Development of New Organic Salts as Versatile Materials for Catalysis, Ionic Liquids and Carbon-Nanomaterials

Habilitationsschrift

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In der vorliegenden kumulativen Habilitation sind die Arbeiten enthalten, die am Institut für Organische Chemie der Technischen Universität Clausthal während einer Juniorprofessur von 2003 bis 2009 durchgeführt wurden.

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Abstract

The presented work deals with the development and application of new organic salts. The work is focusing mainly on salts containing imidazolinium and amidinium cations. These species are less represented in the literature compared to their unsaturated imidazolium analogues, despite the fact that they have high potential in many applications, which will be discussed in this work.

During this work it was possible to develop the nearly unexplored field of imidazolinium based metal free Lewis acids in synthesis. Metal-free Lewis acids are part of the research area of non-covalent organocatalysts. The catalysts were applied to synthetic important reactions and were even suitable to activate thiocarbonyl groups and thiiranes. Furthermore, imidazolinium-dithiocarboxylate inner salts were introduced as novel organocatalysts for asymmetric catalysis. The chiral catalysts were applied to a range of synthetic important asymmetric reactions to prepare enantiopure compounds. It was shown that the imidazolinium moiety has a weak Lewis acidity and the dithiocarboxylate group functions as a Lewis base. In case of the Staudinger reaction excellent yields and *ee´s* were obtained.

Next, imidazolinium salts with hydrogen at the C-2 position were transformed into carbenes with a base and used as Lewis base catalysts. A structural and conceptual novel camphor based carbene was developed giving excellent *ee´s* in the Wynberg reaction. It was also possible to show for the first time that hindered Brønsted bases can act as Lewis base catalysts, which was utilized in the Staudinger and Wynberg reaction. Also new chiral carbene ligands, which are incorporating one or two hydroxy groups, were developed.

In addition, new chiral and achiral ionic liquids, which are stable in the presence of strong bases, based on imidazolinium cations were prepared. The new ionic liquids incorporated also ligator atoms, which makes it possible to apply these new liquids in reactions involving Grignard reagents. The asymmetric addition of Grignard reagents to aldehydes was investigated in the beginning. In addition, the new liquids were suitable chiral shift reagents.

Finally, organic salts based on CpFe(arene) cations were used to develop a new route to prepare carbon nanostructures on a large scale. In order to prepare the novel nanostructures, the salts were pyrolysed. Different metal complexes led to various nanostructures of carbon, like carbon nanotubes, fibers and other forms.

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1. Introduction

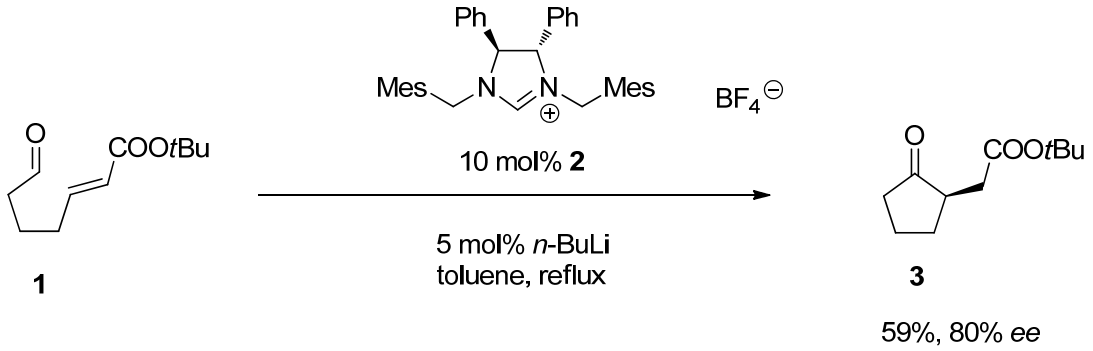
This habilitation was focusing mainly on the development of new organic materials based on organic salts and their application in synthesis and catalysis. It is possible to categorize the application of the presented new salts in section 2 into four fields. The first three deal with the application of new amidinium salts and their application as organocatalysts, ionic liquids and carbene ligands. The last shows the use of CpFe(arene) salts for the synthesis of new carbon nanomaterials. Hence, this introduction is giving a brief overview for these research fields.

1.1 Organocatalysis

During the second half of the last century the research area of asymmetric catalysis was dominated by the application of metal complexes. With different metals, ligands and oxidation states it is possible to tune selectivity and asymmetric induction.[1,2] In many examples the metal is a Lewis acid.[3] However, in nature half of the enzymes catalyzing an asymmetric transformation contain no metals. Thus, when it was shown, that simple L-proline can catalyze an intermolecular aldol reaction in high yield and enantiomeric excess,[4] the research field of asymmetric organocatalysis attracted an increased attention during the last 9 years.

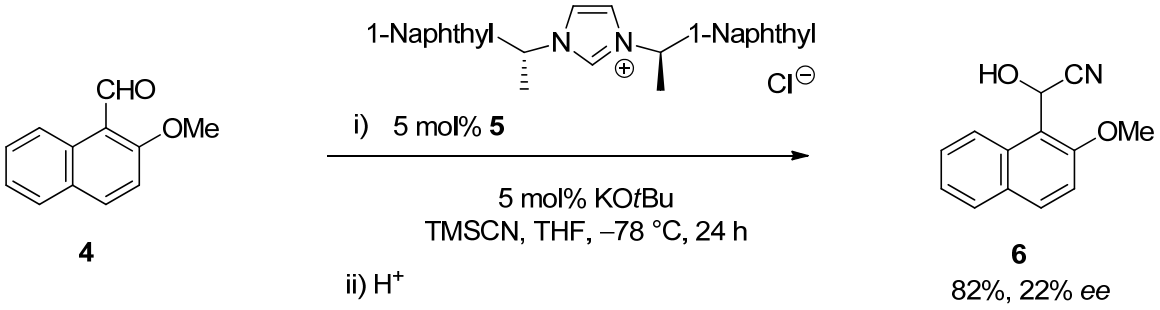
Recently, Dalko has published a second excellent review article about the field of organocatalysis.[5] In addition, Berkessel and Gröger have summarized the topic of asymmetric organocatalysis in their recently published book "Asymmetric Organocatalysis".[6] It is possible to separate the research area of organocatalysis into covalent and non-covalent catalysis. Examples of covalent organocatalysis are often related to enzyme- or antibody catalyzed transformations. Amino acids,[4,7-10] like L-proline, which functions as an amine based asymmetric class I aldolase mimic and forms an enamine as an intermediate,[11] and secondary amines,[12-15] often in the presence of an equimolar amount of Brønsted acid, are applied. In the latter case the reaction proceeds via an iminium ion as the intermediate. Often excellent *ee*`s were obtained. These types of catalysts for example have been recently applied by MacMillan[16] and Enders[17-19] to prepare carbohydrates in a very efficient way. The list of applications with these catalysts was extended by List[20] and MacMillan[21] independently by using them in a metal-free transfer hydrogenation with Hantzsch esters. Moreover, the carbene catalyzed benzoin and Stetter reactions[22-26] represent a part of the covalent organocatalysis research field. In 2004 Bode[27] and Glorius[28,29] independently developed an

N-heterocyclic carbene catalyzed reaction for the preparation of γ-butyrolactones from *α,β*-unsaturated aldehydes. The application of an enantiopure carbene by Glorius[28] led to an *ee* of 25%. Enantiopure *N*-heterocyclic carbenes have been also used as catalysts for the kinetic resolution of racemic secondary alcohols *via* an acylation reaction in up to 51% *ee*.[30] Recently, Tomioko showed that a carbene derived from the enantiopure imidazolinium salt **2**, could catalyze an intramolecular Stetter reaction in up to 80% *ee* as shown in Scheme 1.[31] Remarkably, the reaction was carried out in refluxing toluene.



Scheme 1

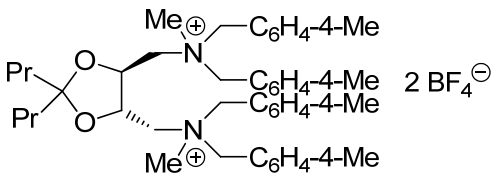
One may also consider the research field of Lewis bases,[32-35] which are often coordinating a silicon atom during a reaction,[36] as part of the covalent organocatalysis research area. Very recently an enantioselective silyl protection of alcohols catalyzed by a Lewis basic amino acid derivative has been reported.[37] Furthermore, Song presented that carbenes derived from imidazolium salts catalyze the $TMSCF_3$ addition to aldehydes.[38] These results were then extended with the TMSCN addition to aldehydes by Song[39] and others.[40-42] Furthermore, it was shown that the TMSCN addition to ketones[42,43] and imines[42-44] can be catalyzed by imidazolium and imidazolinium based carbenes. So far, there has been only one asymmetric version reported as part of the work of Suzuki and Sato.[41] In this rather specific example an *ee* of 22% was obtained as shown in Scheme 2.



Scheme 2

A further example for Lewis base catalyzed reactions is the Staudinger reaction between imines and ketenes. This reaction can be catalyzed by chiral tertiary amines, as shown by Lectka,[45,46] or with planar chiral DMAP analogues developed by the group of Fu.[47]

The field of phase transfer catalysis is a part of non-covalent organocatalysis. The asymmetric induction is introduced by the formation of a chiral ion pair. Next to the family of cinchona related catalysts,[48] two new successful motives of phase transfer catalysts have been developed as depicted below.



(*S*,*S*)-TaDiAS

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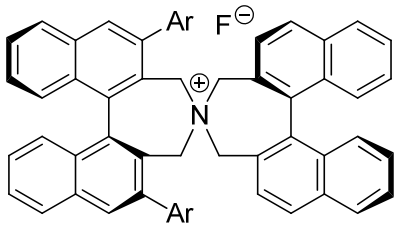

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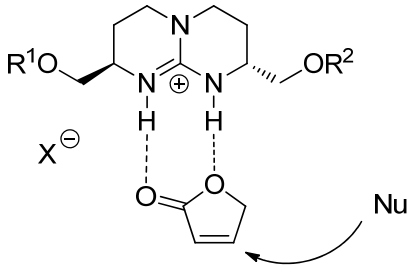
Shibasaki and Ohshima utilized the enantiopure two center phase transfer catalyst **7** in a catalytic Mannich-type reaction of a glycine Schiff´s base.[49] The *ee´*s were up to 82%. Maruoka applied ammonium cations of type **8** as phase transfer catalysts. In case of fluoride as counter anion, it was possible to generate *in situ* nucleophiles from organosilicon compounds.[50]

In addition, catalysts that activate carbonyl compounds *via* hydrogen bonding belong to the area of non-covalent organocatalysis.[51-60] For example, a chiral amidinium salt[51] was catalyzing a Diels-Alder reaction and a chiral guanidinium salt[60] a Michael addition *via* formation of hydrogen bonds (Scheme 3). The observed *ee´*s were rather low. Recently, new systems have been found to give good asymmetric induction.[61]

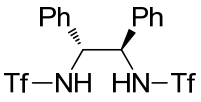


Scheme 3

Rawal[53,62] and Yamamoto[62] obtained excellent *ee´*s with Taddol based catalysts in the hetero-Diels-Alder reaction with aldehydes and an 1-amino-3-siloxydiene. Yamamoto[63] used a

Taddol analogue also as a catalyst in a *N*-nitroso aldol synthesis. An enantiopure binaphthol derivative was applied as bifunctional organocatalyst in an aza-Morita-Baylis-Hillman reaction giving up to 94% *ee*. [64] Next to Jacobsen´s[65] thiourea system, new chiral thiourea analogues have been developed. A bifunctional catalyst incorporating a thiourea group gave in a Morita-Baylis-Hillman reaction up to 92% *ee*,[66] while another gave very good results in the Michael addition to α,β-unsaturated imides[67] and in the Michael addition of malonates to nitroolefines.[68] Recently, thiourea catalysts incorporating a cinchona analogue have been reported.[69,70]

Next to these systems, Jørgensen[71,72] and Mikami[73] demonstrated independently that simple modified chiral diamines **9** and **10** can be used as catalysts. Triflate substituted diamines gave in hetero-Diels-Alder reactions with derivatives of Danishefsky´s diene up to 87% yield and up to 86% *ee*.[73] It was shown, that both NH-groups activate the carbonyl group. Moreover, triflate groups on the diamines were determinative. When a tosyl group was chosen, the catalytic activity dropped dramatically.



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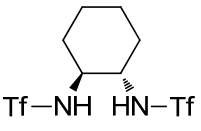

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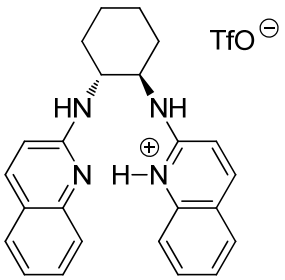
The research field of chiral Brønsted acids started with the work of Johnston and co-workers. The catalyst **11** gave in an asymmetric aza-Henry reaction up to 95% *ee*.[74] Terada prepared catalyst **13**, which is based on an axial chiral binaphthol phosphoric acid, and applied it to the direct addition of acetyl acetone to *N*-Boc-protected aryl imines resulting in up to 98% *ee*.[75] Parallel to Terada, the group of Akiyama used an analogue of this type of catalyst in a Mannich-type reaction of aldimines with silyl enolates and β-aminoester to obtain the desired products in up to 96% *ee*.[76] The necessity of aryl substituents in the 3,3´-positions in **14** was shown by Akiyama impressively. In case when analogue **12** with only hydrogen at the 3,3´-positions was applied in the reaction, an *ee* of 0% was observed. After these reports several other applications of chiral Brønsted acids have been reported. These were very recently summarized in two review articles.[77,78]



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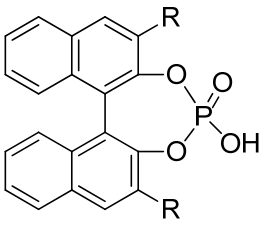


12 R = H
13 R = 4-$NO_2C_6H_4$
14 R = 4-β-(Naphth)-C_6H_4

The field of metal-free Lewis acids is in the literature the least represented class of non-covalent organocatalysts.[79-83] Roles that are normally associated with metals as Lewis acids and as redox agents,[84,85] can be emulated by organic compounds. The field of Lewis acid organocatalyst, compared to other types of organocatalyst is still limited. The number of asymmetric catalyzed examples is small, and the obtained enantiomeric excess is sometimes low. A large number of examples are still promoted by achiral catalysts. Nevertheless, due to the broad variety of possible reactions, which are catalyzed by Lewis acids, possesses this research field a large potential.

Compounds containing carbenium, silyl or phosphonium cations can act as Lewis acids. In addition, phosphorus and silicon based hypervalent compounds display a Lewis acid catalytic activity. Furthermore, ionic liquids, organic salts with a melting point below 100 °C, have shown the ability to catalyze a group of reactions either in substoichiometric amount or, if used as the reaction medium, in stoichiometric or even larger quantities. The solvents can be efficiently recovered after the reaction. Ionic liquids will be briefly discusses in section 1.2.

Metal-free Lewis acids are incorporating a Lewis acidic cation or a hypervalent center. Lewis acids are considered to be species with a vacant orbital.[86,87] Nevertheless, there are two successful classes of organocatalysts, which may be referred to as Lewis acids, but are categorized into another class. The first type is the proton of a Brønsted acid catalyst, which is the simplest Lewis acid. The obtained enantioselectivities are due to the formation of a chiral ion pair, which an example has been discussed above for compounds **11-14**. The other type are hydrogen bond activating organocatalysts, which can be considered to be Lewis acids or pseudo-Lewis acids as discussed above for catalysts **9** and **10**.

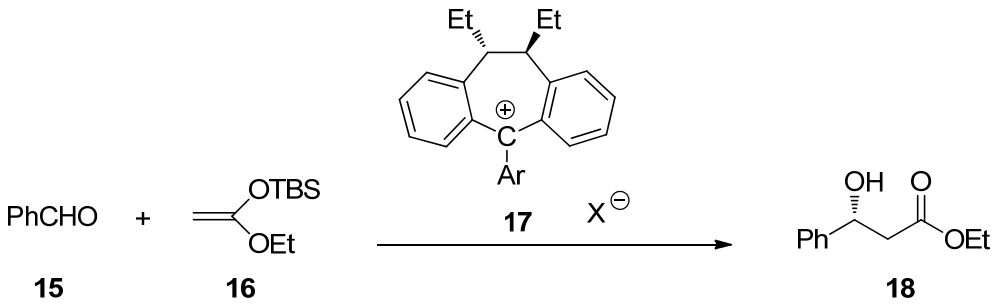
There are some types of organic cations which cannot be placed under the headline of Lewis acid organocatalysts. For example, one type is the chiral guanidinium salt shown in Scheme 3,

which has been used as a catalyst[60] in the Michael reaction. Due to the mode of activation as shown in Scheme 3, this salt belongs to the hydrogen bond activating organocatalysts.

Another type would be ammonium cations of the types RNH_3^+, $R_2NH_2^+$ or R_3NH^+, which could be considered to be Brønsted acids or hydrogen bond activating organocatalysts. Fully substituted ammonium cations, R_4N^+, could interact with a carbonyl group lowering the electron density of its carbon atom. Yet, since the ammonium cation does not possess an empty orbital to take up an electron pair, it is not a Lewis acid. However, enantiopure ammonium salts have been used very efficiently in asymmetric phase transfer catalysis, which has been reviewed.[48,50,88-95]

Next to silyl cations, also hypervalent silicon compounds are Lewis acids. The concept of hypervalent silicon compounds belongs strictly speaking to the class of Lewis base catalysis. However, since a Lewis base forms *in situ* with a silicon atom containing reagent or $SiCl_4$ an intermediate, which functions as a Lewis acid to activate substrates during the reaction, it is also possible to place these reactions to the field of Lewis acid catalyzed reactions. Since silicon is a semimetal we leave it up to the reader to decide whether silicon catalysts should be considered as organocatalysts. Another semimetal is boron, which has been used for a long time as Lewis acid, e.g. BF_3, and of which enantiopure derivatives have been applied very successfully. Asymmetric boron catalysts have been reviewed.[96-99]

The example of a chiral triarylmethyl cation **17**, catalyzing an asymmetric Mukaiyama aldol addition, is the reaction with the highest reported *ee* of 38% for a carbo-cation-based Lewis acid (Scheme 4).[80]



Scheme 4

The highest reported *ee* for a chiral silyl cation catalyst is 54%.[100] The trialkyl silyl cation was prepared from (–)-myrtenal and was applied in Diels-Alder reactions with α,β-unsaturated esters.

A full review on the field of Lewis acid organocatalysts has been attached as copy to the appendix. Sereda, O.; Tabassum, S.; Wilhelm, R. "Lewis Acid Organocatalysts." *Top. Curr. Chem.* **2009**, DOI: 10.1016/j.tetasy.2009.09.015.

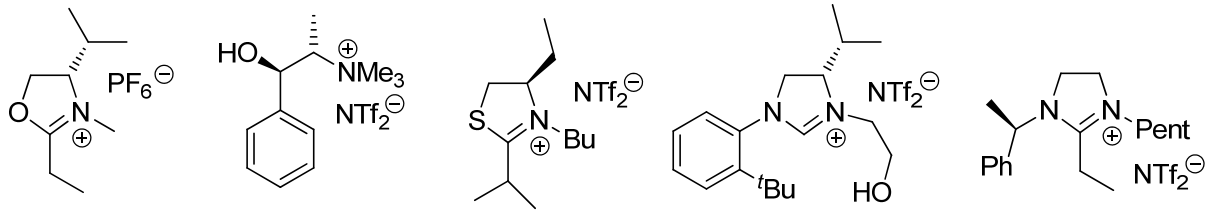
1.2 Ionic Liquids

The research field of ionic liquids, which are salts that have by a definition suggested in 1914 by Paul Walden a melting point below 100 °C, has attracted much interest in recent years as novel solvents for reactions and electrochemical processes.[101] Some of these liquids could be expected to be "green solvents" in case their production process is also green and that they are not toxic or harmful to biological systems.[102] An additional advantage is the efficient recovery of some of these salts. However, in a few examples it is also possible that the ionic liquids are not inert and react with some reagents,[103-105] which could be a disadvantage in some applications. The range of ionic liquids based on various combinations of cations and anions has dramatically increased, and continuously new salts[106-109] and solvent mixtures[110,111] are prepared.

There have been recently several reviews about the preparation and application of chiral ionic liquids.[112-114] Next to chiral ionic liquids also many chiral organic salts are known, which have often a melting point over 100 °C. Compounds like chiral guanidinium salts, which have been used as a organocatalyst,[60] could be mentioned. Also asymmetric phase transfer catalysts, which have been reviewed,[48,50,88-95] are chiral organic salts. Furthermore, the large group of chiral NHC precursors for ligands in metal catalysis[115,116] or for carbene organocatalysis[117,118] are chiral organic salts. In some cases these salts may have a melting point below 100 °C and can be considered to be chiral ionic liquids.

Early ionic liquids have been prepared from organic cations and $AlCl_x$ anions.[119] Since $AlCl_3$ was present in these liquids, they were used as catalysts in Lewis acid catalyzed reactions. Also many of the recent ionic liquids, which incorporate moisture stable inert anions, have been used as solvents for catalytic reactions.[113,120-123] However, it is also known that these ionic liquids are capable of catalyzing reactions, either in substoichiometric amounts or as reaction medium.[124] Due to this relatively strong interaction[125] of the ionic liquids with substrates compared to other solvents, the research in chiral solvents revived.

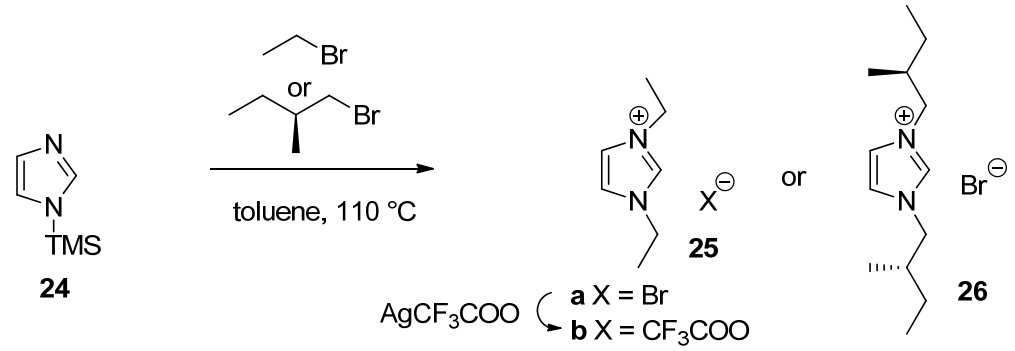
The research field of chiral ionic liquids should not be mistaken with field of task specific ionic liquids, where a common catalytic moiety is attached to a cation. In this field recently excellent *ee´*s were reported.[126] Next to a variety of other cations, especially imidazolium cations, also a few ionic liquids based on imidazolinium cations are known.[101] Beside a few straightforward chiral imidazolium based ionic liquids,[127] the chiral ionic liquids depicted below have been recently described. Salts **19** and **20** have been reported by Wasserscheid and Bolm.[128] While salt **19** proved to be unstable under acidic conditions, salt **20** was stable. The formation of diastereomeric ion pairs of **20** with a racemic mixture of Mosher´s acid sodium salt was shown *via* ^{19}F-NMR spectroscopy. Salts **21**[129] and **22**[130] also interact with a racemic mixture of deprotonated Mosher´s acid. Recently, salt **23** was prepared and applied as a phase transfer catalyst.[131] However, no asymmetric induction was observed. NMR studies with **23** and racemic Mosher´s acid were not carried out. So far, there has been no example of a chiral cation-based ionic liquid giving an asymmetric induction in reactions above 5% *ee*.[127] The only exception is salt **20** with OTf^- as the counter anion. This salt was used in a Baylis-Hillman reaction leading up to 44% *ee*.[132] The asymmetric induction is probably due to the formation of a chiral ion pair. The hydroxy group in the salt was essential for the asymmetric induction.



19 **20** **21** **22** **23**

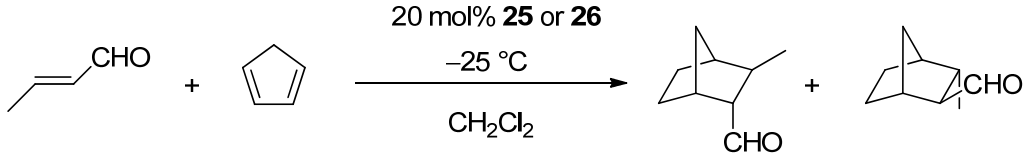
Very recently the group of Leitner reported a chiral ionic liquid, which resulted in up to 84% *ee* in an aza-Baylis-Hillman reaction.[133] The ionic liquid was based on chiral dimalatoborate anions, and it was shown, that the *ee* decreased dramatically, when solvents were added or the ionic liquid was not used at least in equimolar amounts.

Next to these recent examples, Howarth *et al.*[83] reported in 1997 the preparation of ionic liquids **25** and **26**. They showed, that imidazolium cations can be used as Lewis acid centers in catalytic amount rather than as solvent (Scheme 5). The bromide salts **25a** and **26** were prepared by a literature procedure[134] from TMS protected imidazole **24** and ethyl bromide or (*S*)-1-bromo-2-methylbutane in refluxing toluene in 46% and 21% yield, respectively. Salt **25a** was converted into salt **25b** with $AgCF_3COO$ in 89% yield.



Scheme 5

The salts were investigated in the Diels-Alder reaction of crotonaldehyde with cyclopentadiene (Scheme 6). The obtained yields were between 35 and 40% with an *endo*:*exo* ratio of 90:10. The control reaction without the salt at −25 °C gave no product. The observed *ee* with the enantiopure salt **26** was less than 5%. Nevertheless, this was the first example, which showed that chiral imidazolium based ionic liquids can be used in substoichiometric amounts as Lewis acid catalysts.

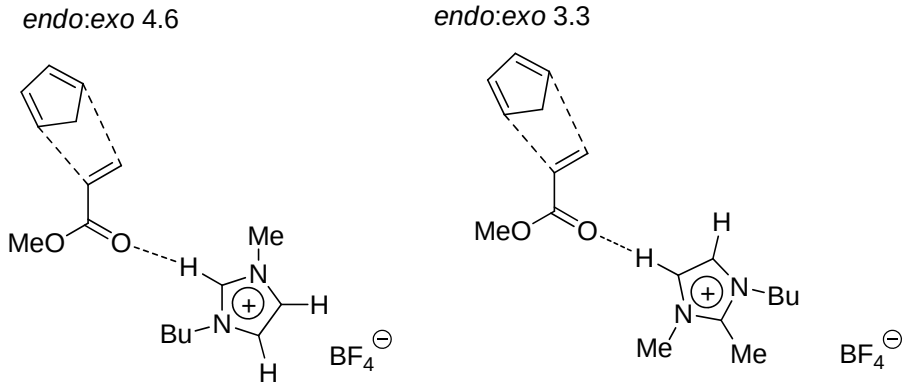


Scheme 6

The use of moisture stable ionic liquids as solvents in the Diels-Alder reaction has also been carried out, and in all examples an enhanced reaction rate was observed.[135,136] The application of pyridinium based ionic liquids allowed the utilization of isoprene as diene.[137] The chiral ionic liquid [bmim][L-lactate] was used as a solvent and accelerated the reaction of cyclopentadiene and ethyl acrylate, however, no enantiomeric excess was observed.[136] In addition, several amino acid based ionic liquids have been recently tested in the Diels-Alder reaction. Similar *exo*:*endo* ratios were found but the product was obtained as racemate. The ionic liquids were prepared by the addition of equimolar amounts of HNO_3 to the amino acids.[138] Furthermore, an enantiopure imidazolium salt incorporating a camphor motive was tested in the Diels-Alder reaction. No enantiomeric excess was found.[139]

In order to investigate the origin of the catalytic activity of imidazolium based ionic liquids, the group of Welton[140] performed further studies, and it was proposed that hydrogen bond activation plays an important part in the activation of a dienophile in the Diels-Alder reaction.

This was proposed due to observed hydrogen bonds between the imidazolium cation and the corresponding counter anion in the salt. The reaction of methyl acrylate in the ionic liquid [bmim][BF_4] with cyclopentadiene gave the product in 72 h at 25 °C in 85% yield. When the C2-methylated salt [bm_2im][BF_4] was applied as solvent, a similar yield of 84% was obtained, however, the *endo*:*exo* ratio changed from 4.6 to 3.3. This was attributed to weaker hydrogen bond formation with the C4 and C5 protons compared to the C2 proton in the first salt (Scheme 7).



Scheme 7

This would place imidazolium based ionic liquids more to the hydrogen bond activator organocatalysts. However, further studies by the group of Dyson showed that ,when salt analogues with [NTf_2] as the counter anion were used in the reaction, the salt with a methyl group at the C2 position gave a better *endo*:*exo* selectivity, indicating that hydrogen bond capability is not the only reason for the activity of the imidazolium ionic liquids, and other variables, like π-orbital interactions have to be taken into account.[141] Recent calculations for an imidazolium salt showed, that the hydrogen bond of a C2-H of the imidazolium cation with a corresponding counter anion is considerably different from that of conventional hydrogen bonds and not as strong as previously considered. The charge-charge interaction of the ion pair was proposed to be the dominant interaction.[142]

A full review on the field of chiral ionic liquids has been attached as copy to the appendix. Winkel, A.; Reddy, P. V. G.; Wilhelm, R. "Recent Advances in the Synthesis and Application of Chiral Ionic Liquids." *Synthesis* **2008**, 999-1016.

1.3 Chiral Carbene Ligands

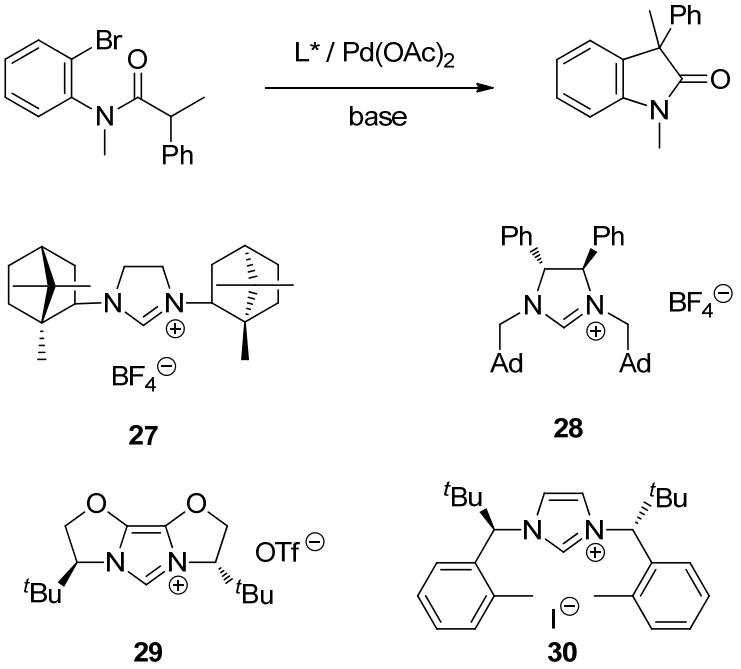
NHCs (*N*-heterocyclic carbenes) have found an important role in various applications in organic chemistry in recent years.[143,144] Because of their nucleophilic character, they can act as ligands for various transition metals, e.g. platinum or palladium. NHCs can substitute phosphanes and other classical ligands such as amines or ethers in metal coordination chemistry. These heterocarbenes show bonding properties similar or even superior to those of trialkylphosphanes and alkylphophinates.[145,146] After the work of Öfele[147] in 1968 a range of metal carbene complexes were synthesized and characterized. Through the work of Arduengo *et al*.,[148] which were incorporating bulky groups in the NHCs, the free carbenes were isolated. By now there are several routes to NHCs known. Most easily available are stable carbenes derived from imidazoles and triazoles, because numerous imidazolium and triazolium precursor compounds can be made along established routes.[149-152] In addition, imidazolinium salt precursors are readily available from secondary diamines and triethyl *ortho*formate.[153]

Recently, Herrmann was covering the synthesis of metal complexes of heterocyclic carbenes in a review article.[143] In general *N*-heterocyclic carbenes can be easily modified and examples of chiral, functionalized, immobilized, water soluble, or chelating-NHC carbene ligands have been reported.[144] A review concentrating only on chiral carbenes was published in 2004.[116]

Imidazolium based carbene ligands were applied in the Heck coupling of aryl bromides and chlorides, which was reported by the group of Herrmann with an exceptional low catalyst loading and excellent yields.[154] In addition, the same group demonstrated that carbenes, derived from imidazolium precursors can be applied in the Suzuki reaction with chloroarenes at room temperature.[155] The scope of this reaction was extended by the work of Glorius, who applied new imidazolium based carbene ligands in order to couple sterical hindered chloroarenes at room temperature.[156]

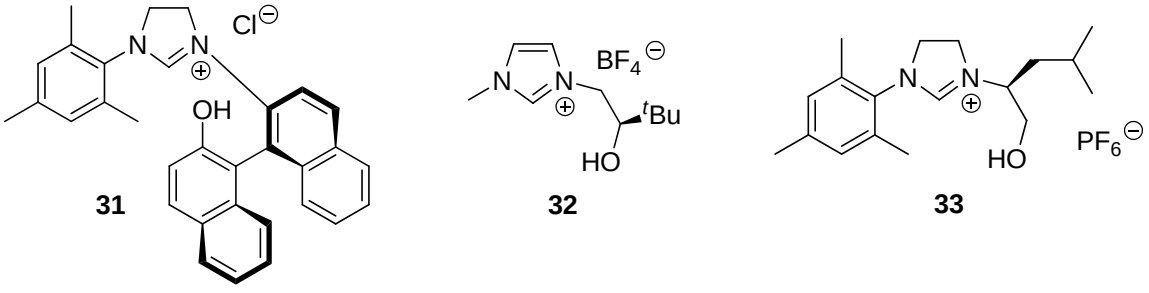
Imidazolinium based carbenes are more basic than the imidazolium derivatives and can be even stronger ligands. They have been for example applied in the palladium-catalyzed amination of aryl halides.[157,158] The application of imidazolinium based carbenes in asymmetric catalysis was reported for example by Hartwig.[159] It was possible in an intramolecular α-arylation of an amide with the carbene ligand derived from salt **27** to obtain a yield of 74% and an *ee* of 57% (Scheme 8). Another system was recently published by Aoyama *et al.*[160] yielding the oxindole in 62% yield and 61% *ee* with salt **28** as the precursor

(Scheme 8). Glorius *et. al*[161] employed oxazoline based imidazolium salt **29** and obtained the product in an excellent yield of 95% but with a moderate *ee* of 43%. Recently, the group of Kündig[162] developed the ligand **30**, which gave the product in 99% yield and 94% *ee*.



Scheme 8

In addition, chiral[163] imidazolinium based carbenes next to achiral[164] carbenes have been also applied in olefin metathesis reactions. An interesting bidentate carbene ligand **31** incorporating a hydroxy group was recently described by Hoveyda[165] and applied with ruthenium in an asymmetric olefin metathesis to give up to 96% *ee*. The carbene ligand was also investigated in a copper-catalyzed allylic alkylation, which gave the desired product in up to 98% *ee*. Furthermore, the group of Polly Arnold was synthesizing salt **32** and isolated a Cu(I) complex with this carbene ligand.[166,167] The complex was used as a catalyst in a diethyl zinc conjugated addition on cyclohexenone resulting in an *ee* of up to 51%. Very recently the group of Mauduit[168,169] was reporting the synthesis of salt **33** and various analogues based on different amino alcohols. The salts were used as carbene precursors in the Cu(II) catalyzed diethyl zinc addition to cyclohexenone and *ee´*s of up to 93% were achieved.



The development new chiral NHCs is desirable, since so far NHCs are giving often in some asymmetric catalyzed reactions a lower asymmetric induction compared to phosphane based ligand systems.

1.4 Carbon Based Nanomaterials

Carbon based nanostructures like single walled carbon nanotubes (SWCNTs) and multi walled carbon nanotubes (MWCNTs) have attracted significant scientific attention in recent years, due to their potential as unique electronic, magnetic and mechanically robust materials.[170-172] Nanotubes containing metals[173] have additional potential as magnetic particles, contrasting agents, protecting cloaks, catalysts, and in other applications. Furthermore, potential biological applications of carbon nanotubes have captured much imagination.[174,175] There have been a few investigations concerning the use of carbon nanotubes for biological purposes and the introduction of carbon nanotubes into biological systems.[176-181] For example very recently short SWCNTs were reported to be capable to transport proteins and oligonucleotides into living cells.[182] Ammonium functionalized MWCNTs were found to be incubated in HeLa cells without causing cell death.[183] Moreover, polyethylene imine-grafted MWCNTs were able to immobilize DNA, which might lead to efficient gene delivery systems.[184]

SWCNTs are commercially available for 50$/g (MER Corporation) and MWCNTs are available for 4$/g (Sun Nanotech Co Ltd). The tubes can be prepared by several established procedures. One procedure is arc discharge,[185,186] which is an energy- and hardware-intensive technique. Furthermore, there are carbon vaporization deposition (CVD),[187,188] and plasma enhanced chemical vapor deposition techniques available, which are giving carbon nanotubes in high yields.[189-191] Additionally, it is known that pyrolyzing organometallic precursors can give carbon nanotubes.[192] Also, to the numerous published work for the preparation of carbon nanotubes, the problem of purifying,[193-196] opening,[178,197] closing[178,197] and cutting[198,199] the tubes has been addressed in many publications. Despite the large number of published work about preparing carbon nanotubes is this field still in its infancy. It is now possible to prepare selectively SWCNTs or MWCNTs, however, the distribution of diameter and length of the tubes is in many experiments still considerably broad. Furthermore, it is so far not possible to prepare tubes with only one helicity. In addition, the problem to synthesize selectively tubes with a defined number of walls has not been addressed at all to this point.

One application of filled carbon nanotubes with magnetic material would be in the field of magnetic decantation. Although magnetic decantation or filtration has been known for a couple of decates,[200] just recently the application of this technique has been reported more frequently. Schüth *et al*.[201] were preparing ordered mesoporous carbon with surface grafted magnetic cobalt particles, which was loaded with 1% palladium, and used the material as a heterogeneous catalyst in the hydrogenation of octane. The catalytic material was separated with the help of a magnet. In addition, Tsang *et al*.[202] were reporting the application of carbon-encapsulated iron-nickel particles loaded with 5% palladium. After the heterogeneous hydrogenation of nitrobenzene, the catalytic material was separated from the product by applying an external magnetic field.

Recently, polymer coated maghemite (γ-Fe_2O_3) nanoparticles[203] or polymer resins with incorporated maghemite nanoparticles,[204] both functionalized with an NCN heterocyclic carbene palladium catalyst, were recovered after their application in a Suzuki reaction. The catalyst was recycled by the application of a magnet in both examples. An NCN heterocyclic carbene palladium complex was also directly attached to maghemite nanoparticles *via* a spacer and applied in the homogenous catalysis of the Suzuki, Heck and Sonogashira cross-coupling reaction.[205] When the palladium complex was replaced by lipase, an enzymatic resolution of racemic carboxylates was carried out.[206] In addition, functionalized magnetite nanoparticles (Fe_3O_4) were used as support for a chiral ruthenium catalyst in the asymmetric hydrogenation of aromatic ketones.[207] $CoFe_2O_4$ nanoparticles coated with a cationic rhodium complex were applied in a hydroformylation.[208] An interesting application of magnetic filtration has been applied recently in order to purify pulsed laser synthesized SWCNTs. Due to a magnetic field, iron impurities were removed this way.[209]

Magnetic nanoparticles have been also recently applied in biological systems.[210-212] For example iron platinum nanoparticles, functionalized with vancomycin, captured *Staphylococcus aureus*.[213] Moreover, enzymes were immobilized on mesoporous silica together with magnetite nanoparticles, without the loss of their enzymatic activity.[214] In addition, silica-magnetite nanoparticles were functionalized with DNA.[215] Living cells were also filled with cobalt ferrite-silica nanoparticles and moved with the help of an external magnetic field.[216]

Some procedures to fill carbon nanotubes with salts and alloys have been reported.[217-220] However, a few recent papers were reporting the filling of carbon nanotubes with magnetic compounds. Here we would like to review only examples, where iron is involved. Large MWCNTs with a diameter of over 300 nm and a rather poor graphitized wall, prepared *via* chemical vapor deposition in alumina membranes, were filled to a large extend with superparamagnetic magnetite (Fe_3O_4) nanoparticles, which were stabilized with a surfactant. The particles were commercially available as a ferrofluid.[221] In addition, MWCNTs were filled *via* wet chemistry with Fe-Ni alloy nanoparticles. The opened tubes were stirred in a solution of ferric and nickel nitrate. The salt particles, which were crystallizing inside the tubes, were then reduced with hydrogen to the alloy nanoparticles.[222] It is also possible to fill MWCNTs *in situ* with iron or iron alloys by applying CVD methods[223-226] or solid state pyrolysis of organometallic compounds.[227] *Via* the solid state pyrolysis also cobalt filled MWCNTs are available.[228,229] The level of filling depends on the organometallic precursor.

Next to the filling of carbon nanotubes with magnetic materials an example was reported, where magnetite nanoparticles were deposited on polymer wrapped MWCNTs, which was used to align the tubes in a low magnetic field.[230] This principle was also used for cyanovaleric acid functionalized MWCNTs decorated with Fe_3O_4 nanoparticles.[231]

In general, the functionalization of CNTs can be achieved by applying reactions used to functionalize fullerenes.[232] However, stronger reaction conditions have to be used. There are examples known, where carbon tubes were fluorinated.[233,234] Furthermore, research has been concentrated to use carboxylic acid groups on the surface and on the open ends of the tubes to attach molecules *via* amide linkages.[235-237] The carboxylic acid groups are created in the cutting and purification procedures, which is achieved by using strong oxidative conditions.[178,193-199] The carboxylic acid groups were also used to attach polymers to the tubes.[238,239] Just a few papers have dealt with the modification of nanotubes *via* electrochemistry.[240,241] Finally, recent work used 1,3 dipolar cycloadditions,[242] and NCN heterocyclic carbenes[243] to functionalize carbon nanotubes. Additionally, the Bingel-Reaction was used to functionalize carbon nanotubes.[244] Next to TEM and SEM the functionalized samples were analyzed with ^{1}H-NMR. Recently, SWCNTs have been also functionalized with alkyl groups and aryl groups by the application of a solution of lithium in liquid ammonia followed by the addition of alkylhalids[245] or arylhalids.[246] Next to covalent functionalizations,

it is also possible to attach pyrene systems non-covalent onto the walls of carbon nanotubes, due to π-π interactions.[247]

Many work has been described in the literature to use carbon nanotubes as support in heterogeneous catalyzed reactions with metal nanoparticles.[171 248-251] In addition, a limited amount of work has been reported about the application of MWCNTs filled with metal nanoparticles in catalysis. The catalytic material revealed a higher selectivity in catalysis.[252-254]

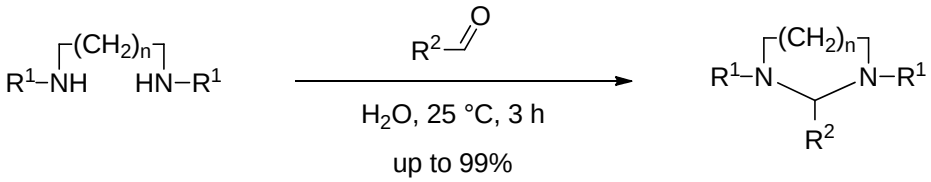
The development of new metal filled carbon nanomaterials is not only desirable for catalysis but also for other applications for example as high potential gas-storage media,[255,256] Li-intercalation materials for batteries,[257] and cold electron field emitters.[258]

2. Results and Discussion

2.1 Synthesis of New Imidazolinium Salts and Their Application as Catalysts

Three different types of potential metal-free Lewis acids for further developing can be identified. Due to limited resources and time, silyl cations and triarylmethyl cations were not investigated. Here, mainly imidazolinium cations were examined due to their easy accessibility and handling. They are stable in the presence of water[259] and under basic conditions in phase transfer catalysis.[131] Of the three outlined possible metal-free Lewis acids the imidazolinium cations possess the lowest acidity. Unlike an ammonium cation, an imidazolinium cation could form to a certain extend a bond[260-263] with its C-2 carbon atom and a free electron pair of an imine, aldehyde or epoxide.

In order to obtain the desired imidazolinium salts, the desired precursors, aminals, were prepared via a new simple procedure. It was possible to synthesize the aminals very easily from diamines and aldehydes by the application of water as reaction medium (Scheme 9).[264] This method gave the products in very good yields and high purities compared to common systems. Hence, an additional purification of the products was not necessary.

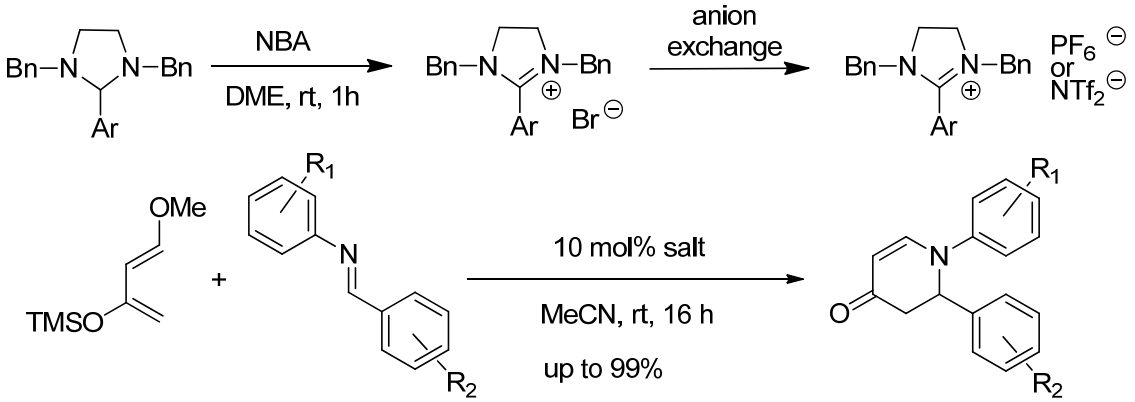


Scheme 9

For full details see attached copy in the appendix. Jurčík, V.; Wilhelm, R. "Preparation of Aminals in Water." *Tetrahedron* **2004**, *60*, 3205-3210.

The so prepared imidazolidines were then transferred into the corresponding imidazolinium salts. Several salts had a melting point below 100 °C. First, only achiral salts were tested as catalysts in an aza-Diels-Alder reaction and in an aza-Diels-Alder reaction with inverse electron demand.[265] The influence of the substituents and counter anions on the catalytic activity was investigated (Scheme 10). The presented test reaction was chosen, because there are so far no catalytic systems known, which give up to 99% *ee* as it is the case for many Diels-Alder reactions or aldol reactions. The salts displayed a high catalytic activity. The influence of the aryl substituents at the C2 position was observed. The more electrondeficient

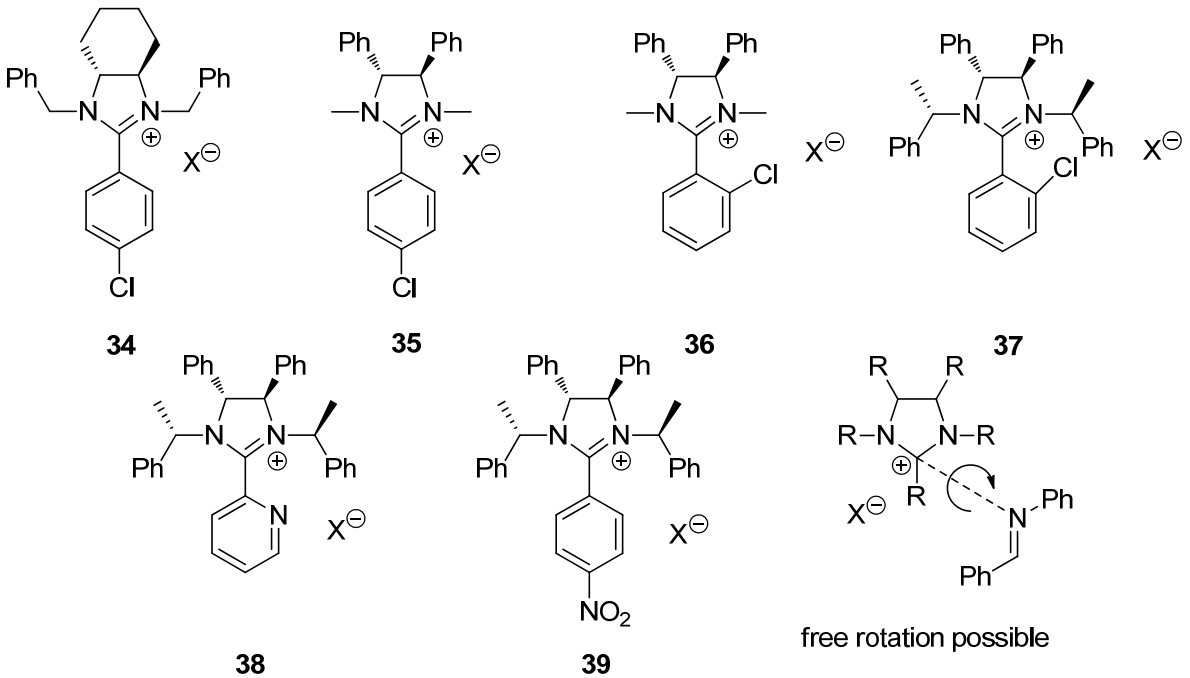
the aryl was, the higher was the activity of the salt. Also, the more lipophilic the counter anion was, the higher was the catalytic reactivity of the salt.



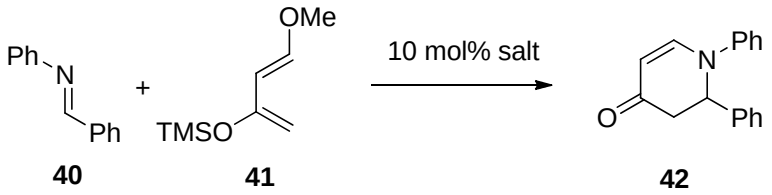
Scheme 10

For full details see attached copy in the appendix. Jurčík, V.; Wilhelm, R. "Imidazolinium Salts as Catalysts for the aza-Diels-Alder Reaction." *Org. Biomol. Chem.* **2005**, *3*, 239-244.

Thereafter, the chiral salts **34-39** were synthesized.[266] A crystal structure of salt **34** showed that the aryl ring was perpendicular to the imidazolinium ring. As shown below, it was anticipated from the beginning that the prepared salts would give in the best case only a small asymmetric induction in a reaction. This is due to the possible free rotation of, for example, an imine during the activation. Nevertheless, the salts were prepared because they are easy to prepare from cheap chiral precursors from the chiral pool. With these salts it was anticipated to optimize reaction conditions for this kind of catalysts.

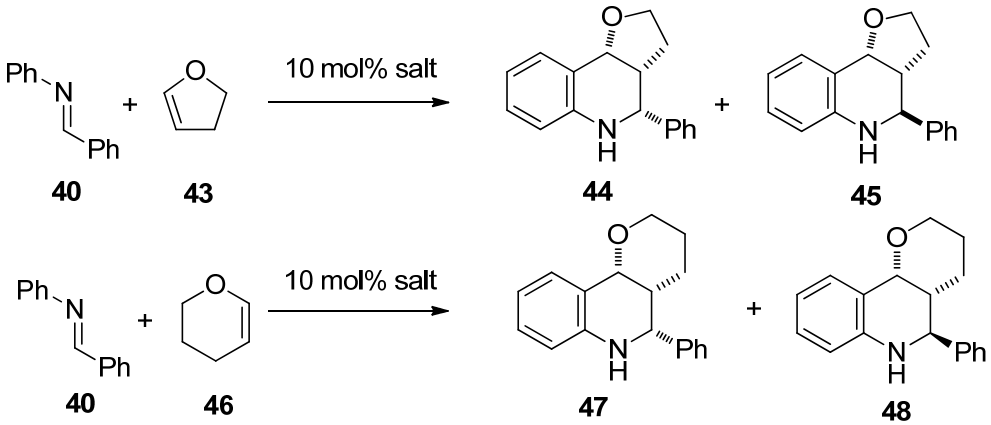


^{19}F-NMR measurements with racemic Mosher´s carboxylate potassium salts showed no splitting of the CF_3 signals. In order to show that there is an interaction between an imidazolinium salt and *N*-benzylidene-aniline, NMR measurements were performed. The latter revealed at room temperature in the ^{1}H-NMR no shifts of the signals. However, in the ^{13}C-NMR the C-2 signal of the imidazolinium salt was shifted up-field, indicating an interaction between the cation and the imine. Salts **34-39** with different anions like PF_6, NTf_2 and $B[3,5\text{-}(CF_3)_2\text{-}C_6H_3]_4$ were applied in the aza-Diels-Alder reaction of *N*-benzylideneaniline (**40**) with Danishefsky´s diene (**41**) under various conditions (Scheme 11).[266] Good catalytic activities were observed, however no asymmetric induction was found. So far, there is no asymmetric variant of the reaction of **40** with **41** known, whether metal or metal-free catalyzed.



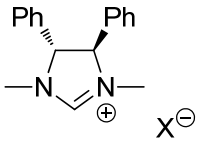
Scheme 11

Thereafter, the salts were tested in the aza-Diels-Alder reaction with inverse electron demand (Scheme 12).[266] So far, there are only two known asymmetric catalyzed reactions of this reaction.[267,268]

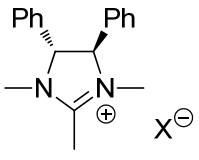


Scheme 12

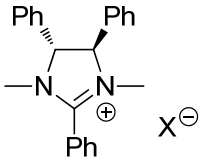
In order to investigate the influence of other substituents at the C2 position of the imidazolinium cations, salts **49-51** were prepared with various counter anions. Salt **51** showed the highest catalytic activity in the reaction of **40** with **43**, while the activity of **49** and **50** was significantly lower.



49

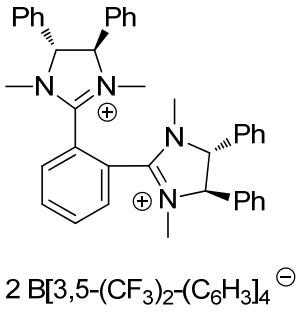


50



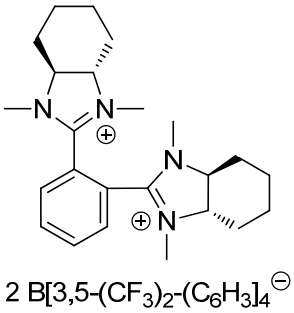
51

Thereafter, imidazolinium salts based on bis-cations were prepared. The cations **52** and **53** were prepared with different counter anions. In ^{19}F-NMR measurements a good splitting of the CF_3-group of racemic Mosher´s carboxylate potassium salt was found.[266] Taking the crystal structure of **34** and MOPAC-PM3 calculations into consideration the configuration depicted below can be assumed. In the shown pocked a free rotation of, for example, an aldehyde would not be possible. However, as can be seen below, the incorporation of two C_2 symmetric units is not favorable for inducing chiral information.



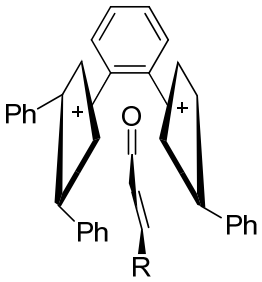
2 B[3,5-(CF$_3$)$_2$-(C$_6$H$_3$]$_4$

52



2 B[3,5-(CF$_3$)$_2$-(C$_6$H$_3$]$_4$

53

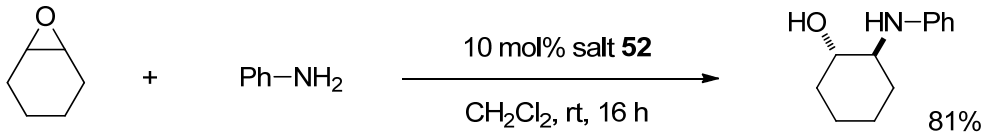


Salts **52** and **53** revealed a much higher catalytic activity in the aza-Diels-Alder reaction with inverse electron demand as the salts with one imidazolinium unit. For comparison 10 mol% of the bis-cation salt and 20 mol% of a mono-cation salt was used in the reaction.

For full details see attached copy in the appendix. Jurčík, V.; Wilhelm, R. "Preparation of New Enantiopure Imidazolinium Salts and Their Evaluation as Catalysts and Shift Reagents." *Tetrahedron: Asymmetry* **2006**, *17*, 801-810.

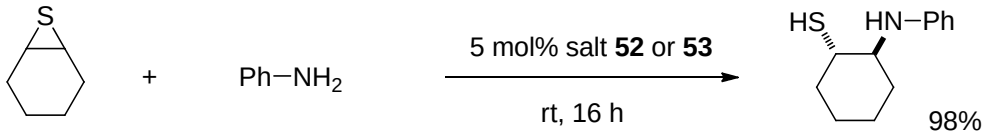
In order to identify a broader range of applications for the salts **52** and **53** further reactions next to the aza-Diels-Alder reaction were tested. First, the addition of aniline to cyclohexene oxide was investigated (Scheme 13).[269] Only a few asymmetric catalytic systems for symmetric epoxides have been reported. All were based on chiral lanthanide or rare earth metal complexes.[270-274] The known systems gave often good *ee´*s, however sometimes, when the epoxides contained no aromatic rests, the *ee´*s were lower. We chose a primary aromatic amine for the test reaction, since they are less reactive than aliphatic amines. The reaction in the absence of catalysts gave after 16 h at room temperature only a yield of 10%. In the

presence of 10 mol% **52**, a yield of 81% was obtained, however, no asymmetric induction was observed. **53** gave a similar result.



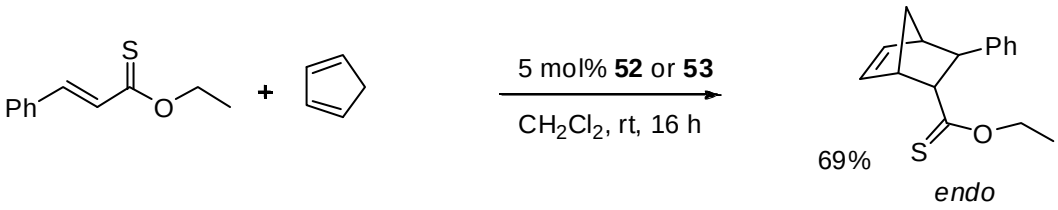
Scheme 13

Next to the ring opening of epoxides, we were also interested in the ring opening of cyclohexene sulfide as shown in Scheme 14.[269] There has been no asymmetric catalyzed reaction reported for the ring opening of thiiranes. An asymmetric catalyzed reaction would be a useful addition to the tool box of the synthetic chemist. In the reaction 5 mol% of **52** and **53** were used in order to obtain the addition product with aniline in up to 98% yield. The product was obtained as racemate. A control reaction without catalyst gave the product after 16 h at room temperature in 12% yield. Due to the low electronegativity of sulfur, it would be difficult to catalyze this reaction with hydrogen bond activation catalysts.[58] On the contrary, Brønsted acids are leading often to desulphurization.



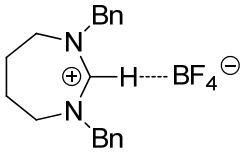
Scheme 14

Finally, a Diels-Alder reaction with ethyl-thionocinnamate[275] and cyclopentadiene as shown in Scheme 15 was investigated with salts **52** and **53**.[269] There has been only one example of an asymmetric Diels-Alder reaction reported involving a thioester. In the latter example O-ethyl crotonthioate was reacted with cyclopentadiene using a chiral bis-mercury complex as a catalyst to give an *ee* of up to 58% with a yield of 44% at –23 °C.[276] A catalytic amount of 5 mol% of salts **52** or **53** gave the novel adduct after 16 h at room temperature in 69% or 63% yield, respectively (Scheme 15). Only the *endo*-product was observed. No asymmetric induction was found according to chiral HPLC measurements. In the absence of a catalyst, no reaction was observed at room temperature. By increasing the temperature to 45 °C the product was obtained in 22% yield after 3 days. The *endo*:*exo* ratio was 13:1.



Scheme 15

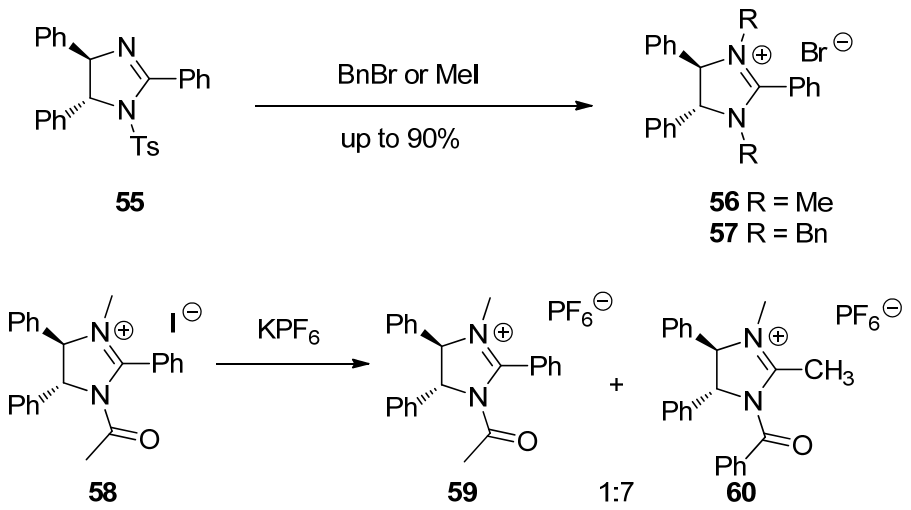
In addition to the bis-cationic salts **52** and **53**, also achiral salts based on six- and seven-membered rings were prepared, and their reactivity was tested.[269] It was possible to show that dihydropyrimidinium salts were slightly more reactive than imidazolinium salts. The reactivity of seven-membered NCN salts however, was significantly higher and as good as that of bis-cations **52** and **53**. This could be explained by taking the different NCN bond angles into consideration. MOPAC calculations showed that in a seven-membered ring the NCN angle is up to 135 °. In smaller and larger rings and in open NCN amidinium salts the angle is smaller. The more the angle diverges from 120°, the less the positive charge is delocalized and the Lewis acid center is hence stronger.



54

In addition, during the synthesis of several other imidazolinium based cations, incorporating a tosyl group or acetyl group, some unexpected results were observed as shown in Scheme 16. These observation are unprecedented so far.[277]

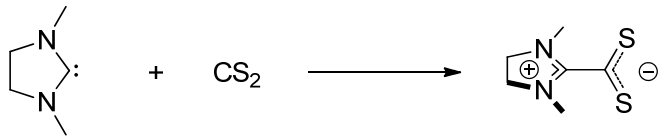
For full details see attached copy in the appendix. Clemens, N.; Sereda, O.; Wilhelm, R. "Unexpected Behaviour of Tosylated and Acetylated Imidazolinium Salts." *Org. Biomol. Chem.* **2006**, *4*, 2285-2290.



Scheme 16

2.2 Imidazolinium-Dithiocarboxylate Inner Salts and Their Application as Novel Catalysts

Imidazolinium-dithiocarboxylates[278-285] belong to the extraordinary class of carbene complexes of nonmetals.[279] They can be formally prepared by the addition of an imidazolinium carbene to CS_2 (Scheme 17). The CS_2 group is tilted almost perpendicularly relative to the imidazolinium ring and may be regarded as a Lewis base center. It cannot function as a good Brønsted base since the pK_a of the corresponding acid has been suggested for an analogue to be ca. –2.[286]

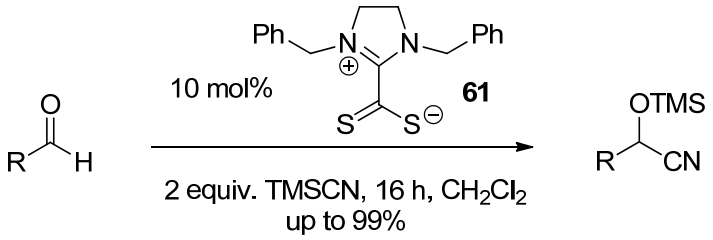


Scheme 17

So far these dithiocarboxylate zwitterions have been applied only rarely as ligands for metal complexes[287-291] or as substrates in [3+2] cycloadditions with electron deficient alkynes.[292] Recently, the group of Demonceau[293] was using CO_2 analogues, imidazolium- and imidazolinium-carboxylates as highly efficient carbene precursors for the palladium catalyzed Suzuki-Miyaura reaction. The fact that imidazol(in)ium-carboxyates decompose back to CO_2 and carbene has been shown by the groups of Louie[294] and Crabtree.[295] When Demounceau[293] was applying imidazol(in)ium-dithiocarboxylates in the Suzuki reaction, the conversion dropped dramatically, which can be explained by the fact that imidazol(in)ium-dithiocarboxylates do not decompose to the carbene and CS_2[279] but can form themselves

complexes with palladium.[287-291] There has been only one report that an inner salt was decomposing to CS_2 and carbene, when sublimed at high vacuum at 165 °C.[296] In case no vacuum is applied, it is known that the inner salts decompose at 230 °C to their thiourea analogues.[297]

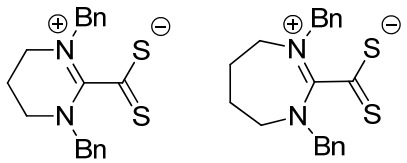
Due to the incorporated Lewis acid and Lewis base centers we were interested, if imidazolinium-dithiocarboxylates can be applied as catalysts for the TMSCN addition on aldehydes. The later reaction is known to be catalyzed by Lewis acids, Lewis bases and bifunctional catalysts. As shown in Scheme 18 the novel organocatalyst **61** gave the desired product in up to 99% yield in 16 h. The catalyst could be conveniently recovered during the purification process.[298]



Scheme 18

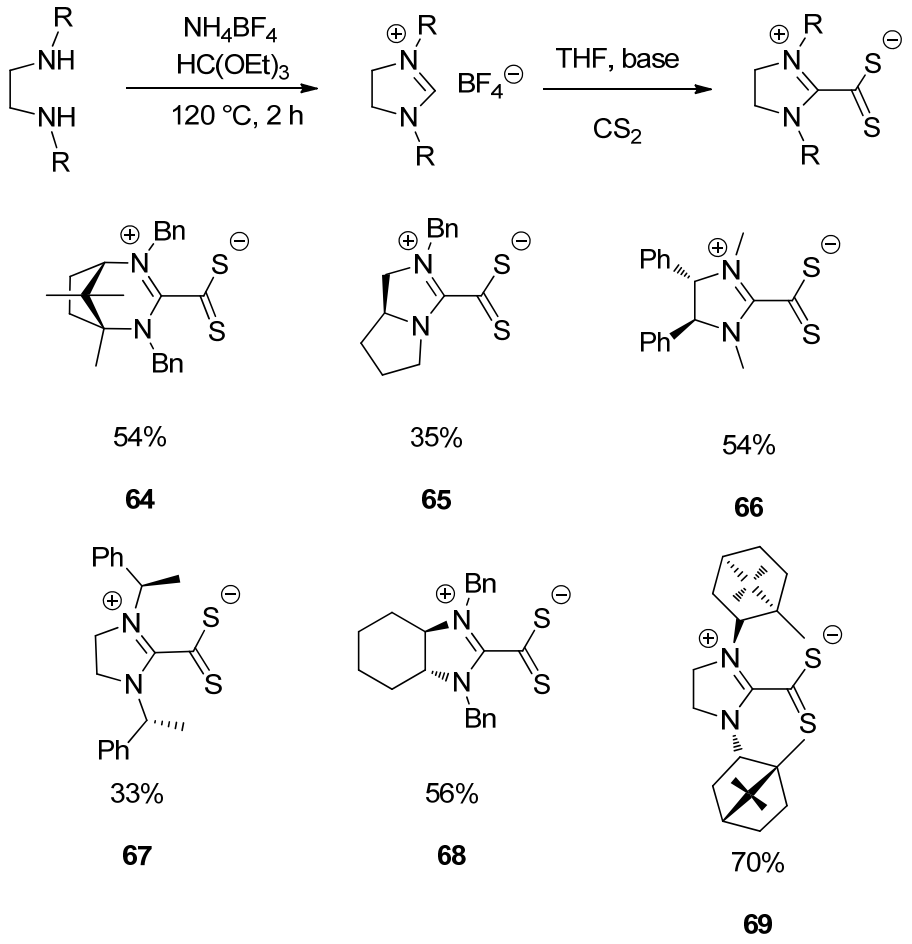
For full details see attached copy in the appendix. Blanrue, A.; Wilhelm, R. "Imidazolinium-Carbodithioate Zwitterions as Organocatalysts for the Cyanosilylation of Aldehydes." *Synlett* **2004**, 2621-2623.

Next to the reactivity study for the TMSCN addition on aldehydes with imidazolinium-dithiocarboxylate zwitterions,[298] additionally zwitterions **62** and **63** were prepared and tested in this reaction.



62 **63**

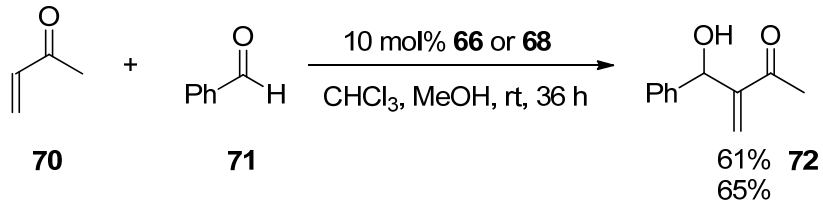
While the six-membered zwitterion **62** had just a slightly smaller reactivity than its imidazolinium analogue, zwitterion **63** did not catalyze the reaction at all, which showed, that the strong positive center is decreasing the Lewis base strength of the dithiocarboxylate unit, necessary to activate the TMSCN.[299]



Scheme 19

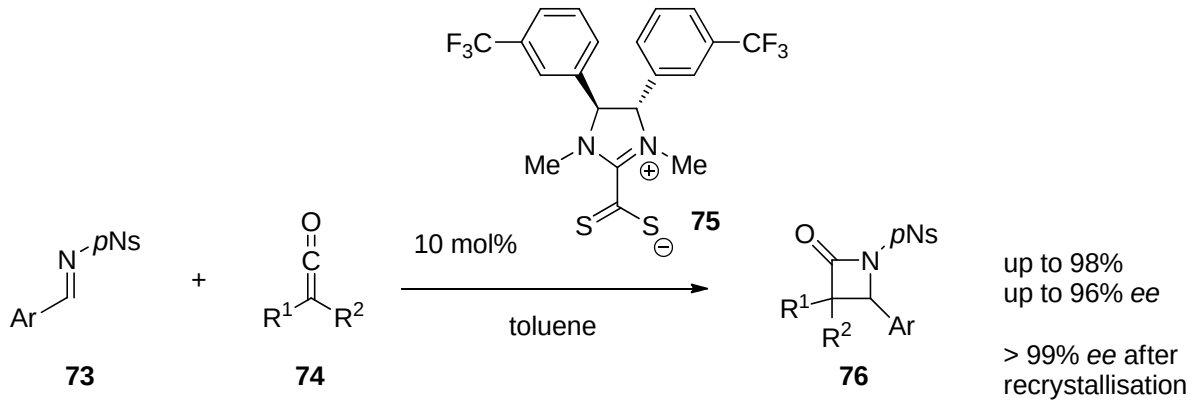
Several chiral zwitterions were prepared as shown in Scheme 19 from corresponding imidazolinium salts.[299] The salts were deprotonated and the resulting carbenes treated with CS_2. The zwitterions were tested in the TMSCN addition to benzaldehyde under various conditions. The *ee´*s were between 0 and 14%. For the reactions 10 mol% of catalyst were used. The highest asymmetric induction was found in unpolar solvents. However, the zwitterions were not totally soluble in these solvents except CH_2Cl_2, which makes it difficult to determine the actual mol% of active catalyst in the unpolar solvent. The reason, why polar solvents led to no asymmetric induction can be explained by a CN^- catalyzed background reaction, which has been investigated by Denmark in more detail.[300] Considering the results of Song[39] the precursor salts of the presented zwitterions were also tested in the TMSCN addition to aldehydes. Several solvents and bases, like *n*-BuLi, KO*t*Bu and KHMDS, were screened for preparing the carbene catalysts *in situ*. The reactions were carried out at −78 °C. Although the carbenes showed a higher reactivity than the zwitterions, no asymmetric induction was observed.

It was also shown that the zwitterions can catalyze the aza-Diels-Alder reaction of Danishefsky´s Diene and *N*-benzylideneaniline at room temperature in 90% yield, however, with no asymmetric induction. In addition, as shown in Scheme 20 the zwitterions **66** and **68** were able to catalyze a Baylis-Hillman reaction. Yields of 61 and 65% were obtained. The presence of methanol was for the reaction essential. The reaction did only proceed with but-3-en-2-one.[299] Other Michael systems commonly used in Baylis-Hillman reactions gave no desired products.



Scheme 20

Due to the observed weak Lewis acidity but strong Lewis basicity of these compounds,[299] we were then concentrating our effort on the Staudinger reaction. Zwitterion **75** was used as a very successful novel organocatalyst in the Staudinger reaction as shown in Scheme 21.[299,301] It was also possible to show that the reaction gave under neat conditions a significant enantiomeric excess, which is remarkable, considering the fact, that normally highly dilute reaction conditions are necessary for this reaction.[302] The present *para*-nosyl group is in general a convenient protecting group compared to tosyl, since a nosyl group can be easily removed from a nitrogen.[303] It was however observed that under the standard conditions, it was not possible to remove the nosyl group from the *β*-lactones, hence, a new procedure was developed in order to remove the group in nearly quantitative yields.[301]



Scheme 21

For full details see attached copy in the appendix. Sereda, O.; Blanrue, A.; Wilhelm, R. "Enantiopure Imidazolinium Dithiocarboxylates as Highly Selective Novel Organocatalysts." *Chem. Commun.* **2009**, 1040-1042.

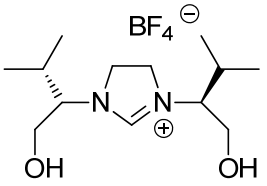
During the investigation of this reaction it was also found that NaHMDS can act as a highly active catalyst for the reaction shown in Scheme 21 giving the desired product in near quantitative yield at −78 °C in less than 5 min.[304] This was the first time that NaHMDS has been used as a Lewis base catalyst.

For full details see attached copy in the appendix. Sereda, O.; Wilhelm, R. "Hexamethyldisilazane Sodium Salt as Highly Active Lewis Base Catalyst for the Staudinger Reaction." *Synlett* **2007**, 3032-3036.

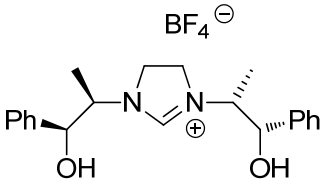
2.3 New Chiral Imidazolinium and Amidinium Salts for Carbene Ligands and Carbene Catalysis

Amino alcohol based salts

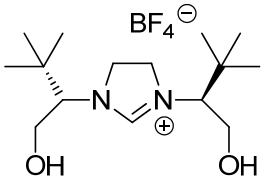
Novel imidazolinium salts like **77**-**80**[305] were prepared from the corresponding diamines, NH_4BF_4 and triethyl *ortho*formate[153] in one step in yields of around 90%. Interestingly, the presence of the hydroxy groups did not have any negative effect. The diamines were prepared from the appropriate amino alcohols and 1,2-dibromoethane. The precursor of salt **80** was isolated *via* the reaction of *trans*-diaminocyclohexane and cyclohexene oxide.[306] Norephedrine for salt **78** is commercially available for a reasonable price.



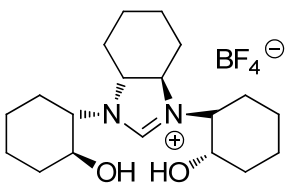
77



78

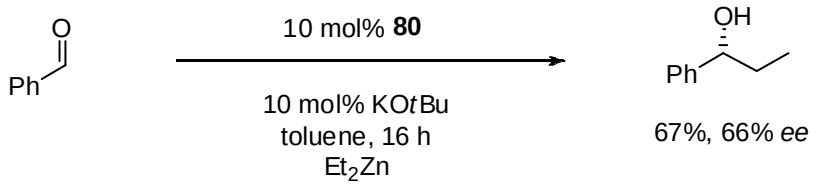


79



80

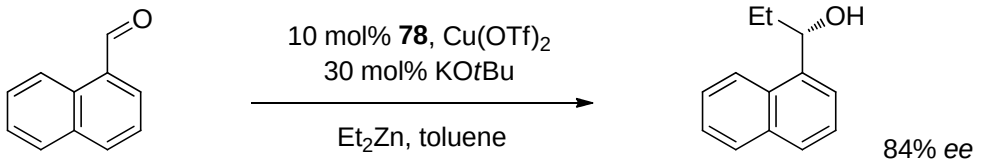
The new salts were evaluated[305] in the diethyl zinc addition on benzaldehyde (Scheme 22). Salt **80** itself did not catalyse the reaction, however, when the carbene was formed by the addition of 1 equiv. KO*t*Bu, the reaction yielded the desired product in 67% yield and 66% *ee* after 16 h. Usage of 2 or 3 equiv. of KO*t*Bu did not had any influence on the result. When 1 equiv. of KHMDS was used, the yield increased to 92%. The mechanism of the reaction has been thoroughly examined for β-amino alcohol ligands.[307,308] In the present case, the carbene unit is probably taking over the role of the amine substituent of a β-amino alcohol. The salt **78** was recovered and detected by NMR after the aqueous work, which proves that the carbenes are stable under the reaction conditions.



Scheme 22

For full details see attached copy in the appendix. Jurčík, V.; Gilani, M.; Wilhelm, R. "Easy Accessible Chiral Bis-Hydroxy Imidazolinium Salts as Shift Reagents and Carbene Precursors." *Eur. J. Org. Chem.* **2006**, 5103-5109.

The reaction was further optimized by screening next to Zn different metals for these carbene ligands.[309] Switching from zinc to a copper Lewis acid center by the addition of $Cu(OTf)_2$ and further screening of carbene analogues of **78**, which are potential tridentate ligands and are based on ready available amino alcohols, made it possible to obtain the desired product in up to 84% *ee* as depicted in Scheme 23. In addition, it was possible to explore the behavior of other metals with these ligands. As expected oxophilic metals like titanium gave the best results. Only a catalyst loading of 3 mol% was necessary. Next to toluene other solvents were screened, however, toluene gave the best results. Salts **77** and **79** gave low *ee´*s indicating that for this reaction it is beneficial that the OH groups are part of an asymmetric center. Other aldehydes were also tested with good results.

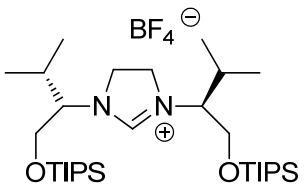


Scheme 23

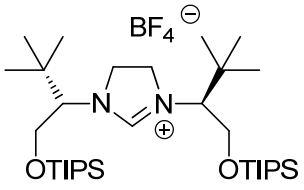
For full details see attached copy in the appendix. Gilani, M.; Wilhelm, R. "New Enantiopure Imidazolinium Carbene Ligands Incorporating Two Hydroxy Groups for Lewis Acid Catalyzed Diethyl Zinc Addition to Aldehydes." *Tetrahedron: Asymmetry* **2008**, *19*, 2346-2352.

Next, these carbene ligands were applied as ligands in Pd catalysed reactions. Although **77-80** can be used in a Pd catalysed Heck reaction, they were not suitable for a Suzuki reaction or for the intramolecular α-arylation of an amide shown in Scheme 24. Therefore, bis-amino alcohols were protected with TIPSCl in quantitative yields and further transformed into the corresponding salts **81-83.** Next to the depicted salts several other analogues were prepared and yields of up to 77% were achieved in the Suzuki reaction.[310]

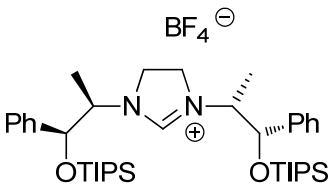
Several salts like **83** showed an unusual behaviour in the ^{1}H-NMR. Although in general the C2-H signal of an imidazolinium salt comes around 8.50 with a BF_4 counter anion in deuterated chloroform, the signal for salt **83** came at 7.40 as confirmed by HSQC with the carbon signal at 155.6. Obviously, the imidazolinium cation is not able to form a hydrogen bond with the BF_4 counter anion due to the sterical surrounding environment. Salt **83** with a chloride counter anion instead of a BF_4 anion was not soluble in chloroform. In deuterated methanol the C2-H signal was observed at 7.42, while in deuterated acetone the signal was at 8.89. An analogue of salt **83**, where the TIPS groups were replaced by TBDMS groups, which are slightly smaller, and a BF_4 counter anion, showed a shift of 7.65 in deuterated chloroform.



81

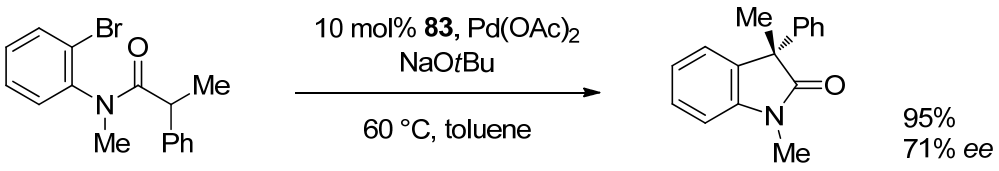


82



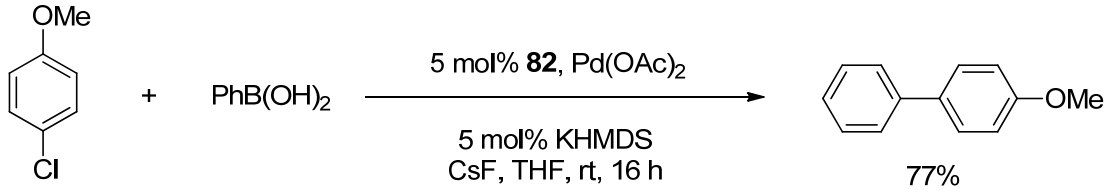
83

The salts were tested[310] in palladium catalyzed cross-couplings. It was possible to apply these carbenes in a palladium catalyzed α-arylation for the preparation of oxindoles, which are an important substructure of biologically active compounds (Scheme 24). The product was obtained with an excellent yield of 95% with an *ee* of 71%.[310] Application of the other two salts resulted in no asymmetric induction, indicating, that it is beneficial that the TIPSO groups are part of an asymmetric center.



Scheme 24

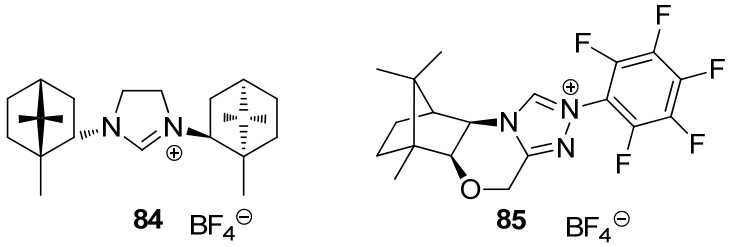
Finally, the reactivity of the salts was tested in an achiral Suzuki reaction with an electron rich chloroarene as shown in Scheme 25. It was possible to obtain the desired product at room temperature with ligand **82** in 77% yield. Only 5 mol% catalyst loading was necessary.



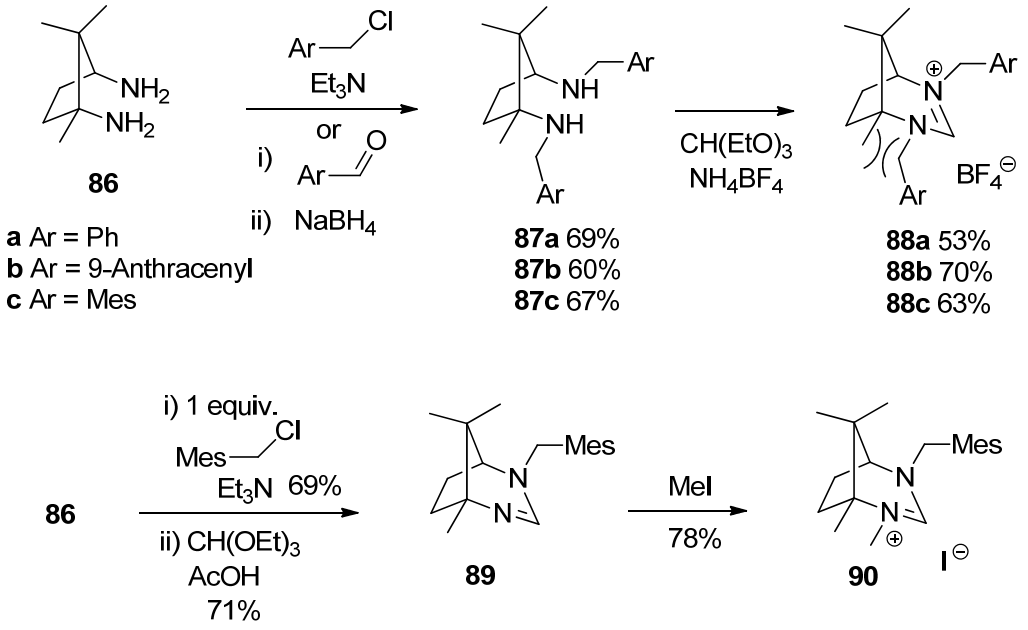
Scheme 25

Camphor based salts

Although camphor is a cheap desirable starting material from the chiral pool, only a few carbene precursors as **1**[159] and **2**[311] have been prepared and successfully used so far in asymmetric catalysis.

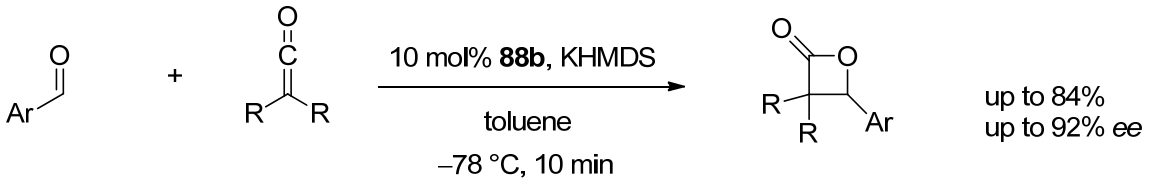


Chiral camphor based carbene precursors of type **88** have not been reported so far (Scheme 26).[312] The NCN unit would be embedded in a rigid bicyclic system being part of a six and seven-membered ring. Hence, the corresponding carbene possess a higher basicity than carbenes with imidazolium or imidazolinium moieties.[313,314] In addition, the free rotation of a substituent next to the C-10 methyl group of the camphor skeleton could be limited due to sterical hindrance, which could provide an asymmetric differentiation in a catalytic reaction step. The diamine **86** can be prepared readily *via* a Schmidt reaction from (+)-camphoric acid,[315] a cheap chiral building block derived from camphor as shown in Scheme 26.



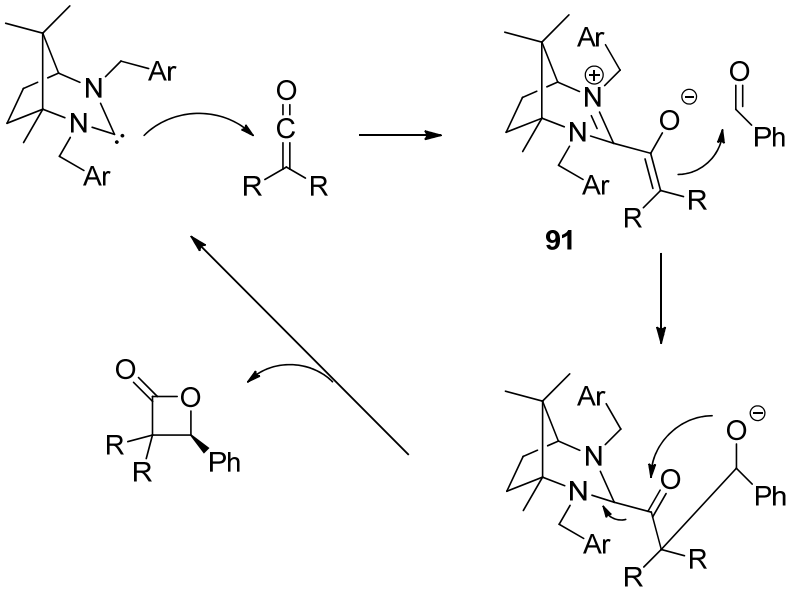
Scheme 26

The new catalysts were applied in the enantioselective Wynberg reaction. The deprotonation of salt **88b** gave a highly active carbene that catalyzed the Wynberg reaction at −78 °C in just 10 min with up to 84% yield and 92% *ee*, which is the highest reported *ee* for this product (R = -$(CH_2)_6$-, Ar = Ph) so far (Scheme 27).[312]



Scheme 27

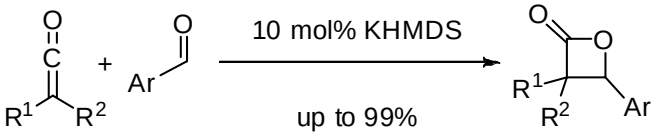
The possible mechanism is shown in Scheme 28. The carbene attacks the ketene. Since the ketene is shielded from one side, the aldehyde can only approach from the side opposite of the C-10 methyl-group of the camphor skeleton. After the new bond is formed, the carbene is released under the formation of the (*S*)-*β*-lactone. It is reasonable to assume that in intermediate **91** the NCN unit and the enolate are not in one plane but perpendicular to each other due to sterical hindrance in analogy to CS_2 adducts to nucleophilic carbenes and other literature reported analogues.[278-280]



Scheme 28

For full details see attached copy in the appendix. Reddy, P. V. G.; Tabassum, S.; Blanrue, A.; Wilhelm, R. "New Enantiopure NHCs Derived from Camphor." *Chem. Commun.* **2009**, 5910-5912.

In addition, it was also possible to show that the hindered Brønsted bases, KO*t*Bu, NaHMDS and KHMDS can function as very active Lewis base catalysts in this reaction. The desired products were obtained in up to 99% yield (Scheme 29).[316]



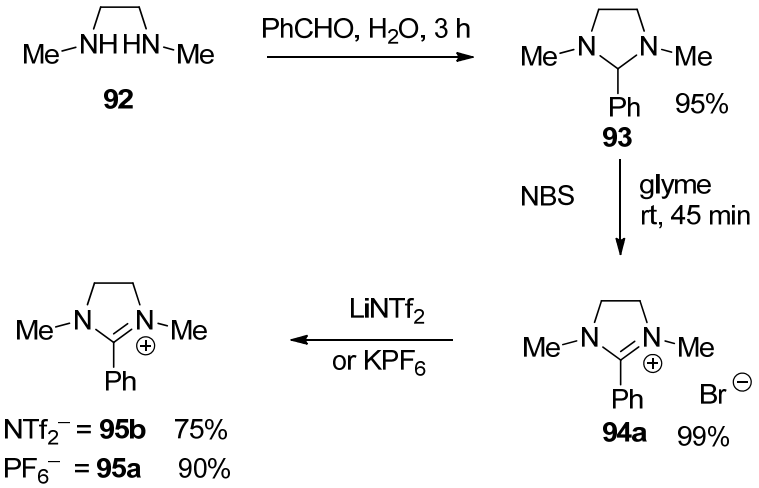
Scheme 29

For full details see attached copy in the appendix. Tabassum, S.; Sereda, O.; Reddy, P. V. G.; Wilhelm, R. "Hindered Brønsted Bases as Lewis Base Catalysts." *Org. Biomol. Chem.* **2009**, **7**, 4009-4016.

2.4 Development of Base Stable and Chiral Ionic Liquids

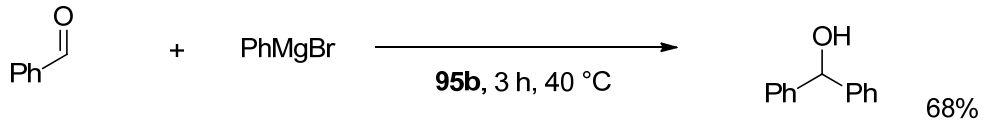
As discussed in section 1, deals the research field of ionic liquids with salts, which have per definition a melting point below100 °C. Obviously several of the presented salts in sections 2.1-2.3 had melting points below 100 °C and can be considered as chiral ionic liquids. It was also possible to show that some of these salts can be applied as chiral shift reagents with Mosher´s carboxylate potassium salt. In this section the synthesis of several new salts is presented, which are being applied as ionic liquids.

While ionic liquids (e.g. [bmim][BF_4]) have become alternative reaction media for a large number of reactions, their application in reactions involving strong bases is often limited due to their easy deprotonation at the C-2 position and even at the 4- and 5-position, which leads to the formation of *N*-heterocyclic carbenes. Therefore, the new salt **95b** was developed (Scheme 30), which had a melting point of 37 °C and once contaminated with reaction educts became a room temperature ionic liquid. Due to an aliphatic backbone and a phenyl group at the C2 atom, a deprotonation should not be possible.



Scheme 30

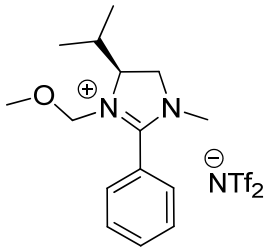
It was possible to show that salt **95b** can be used as ionic liquid and is stable in the presence of medium bases for the Baylis-Hillman reaction and strong bases in the Grignard addition to aldehydes (Scheme 31). A deprotonation and a possible addition to the C-2 center were not detected under the reaction conditions and the ionic liquid could be recycled several times.[104]



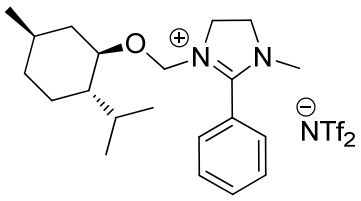
Scheme 31

For full details see attached copy in the appendix. Jurčík, V.; Wilhelm, R. "An Imidazolinium Salt as Ionic Liquid for Medium and Strong Bases." *Green Chem.* **2005**, *7*, 844-848.

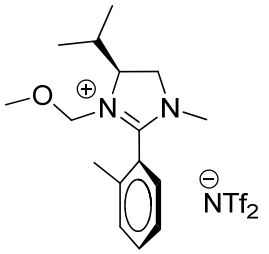
Since salt **95b** is a suitable ionic liquid for the addition of Grignard reagents to aldehydes, chiral analogues like **96** have been prepared.[317] They can be synthesized from an imidazoline and MOMCl. Analogues derived from chiral imidazolines and MEMCl have been also prepared. The oxygen atom of salt **96** could coordinate a magnesium atom of a Grignard reagent, ensuring that the reagent is in close proximity to the asymmetric center of the salt. All salts had a melting point below 100 °C.

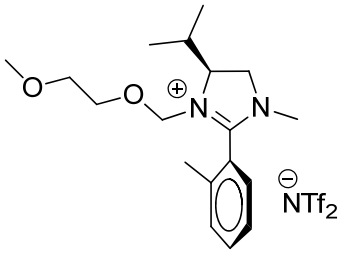


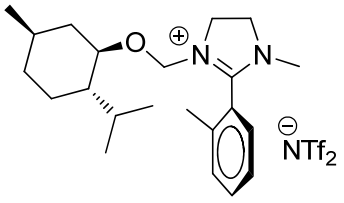
96

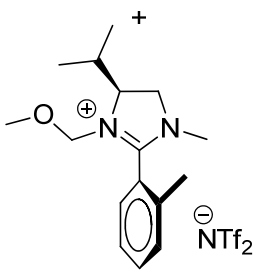


97









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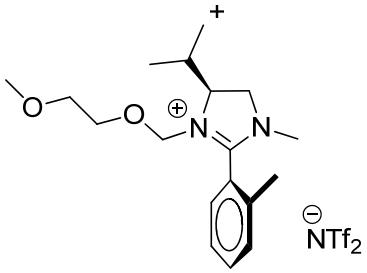

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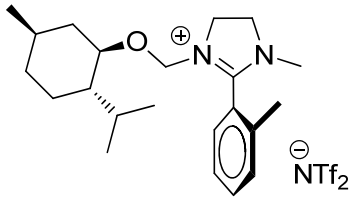


100

Those ionic liquids, which have an *o*-tolyl group at the C2-position of the imidazolinium ring, have besides a central chirality also an axial chirality. The rotation around the axis is sufficiently hindered, which makes it possible to observe in the NMR separate signals for each diastereomer. The diastereomeric ratios for the described ionic liquids were calculated from the ^{1}H-NMR data. The following ratios were observed. 3:2 (**98**), 4:3 (**99**) and 1:1 (**100**). It was not possible to separate the diastereomers. An assignment of the peaks to one specific diastereomer was not possible by NOE. However, it is reasonable to assume for **98** and **99** that the less sterical demanding diastereomer is formed in excess. While a free rotation in salts

98, **99** and **100** is restricted, there is no rotational barrier in the corresponding imidazolines. The tolyl group is locked in the quaternization process and an obviously high rotation barrier prevents free rotation around the C2-C(tolyl) axis because of sterical hindrance between the newly introduced substituent at the N1-atom and the methyl group of the tolyl ring. In order to determine the rotational barrier, IL **98** was heated in d_6-DMSO during the NMR-measurement from rt to 50, 100 and 150 °C in order to evaluate changes in the diastereomeric ratio. However, even at 150 °C no change in the NMR was observed so that one can assume a remarkable high rotational barrier around the imidazolinium - tolyl C-C axis.

While some of the salts gave similar yields in the Grignard addition as with salt **95b**, no asymmetric excess was found. However, they could be used as chiral shift reagents with Mosher´s carboxylate potassium salts. In addition, *rac*-1-phenyl-2,2,2-trifluoroethanol with **101** in $CDCl_3$ also showed no splitting of the C1-proton, but a downfield shift of 0.2 ppm was observed. Results changed drastically when **101** was applied in toluene-d_8. The alcohol's C1-proton signal shifted from 4.38 ppm (without ionic liquid) to 5.62 ppm. Also a splitting of the quadruplett is detectable. The chiral recognition by ionic liquid **101** causes a splitting of about 2.5 Hz. In the ^{19}F-NMR a significant splitting was found. This is the first example, where a chiral ionic liquid could be used as a shift reagent for a neutral compound. Measurements were repeated with enantiomerically enriched 1-phenyl-2,2,2-trifluoroethanol (*S*-enriched, 50% *ee* and 33% *ee*).

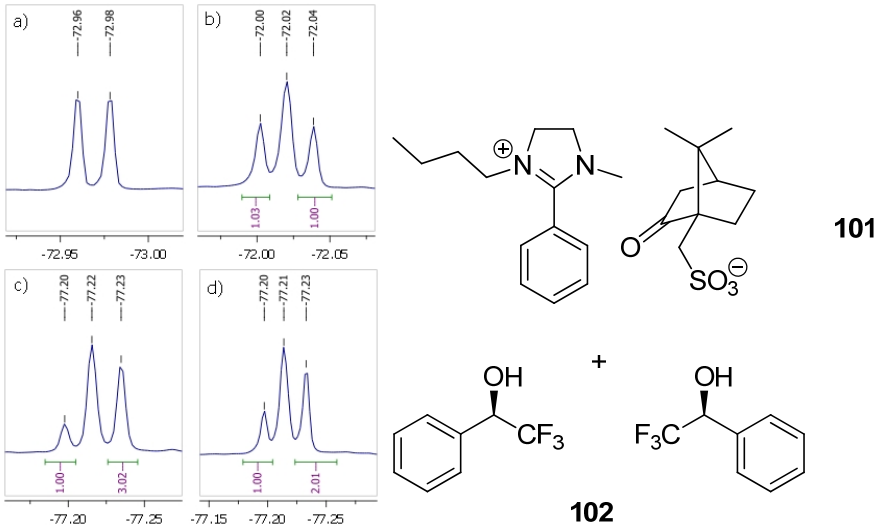
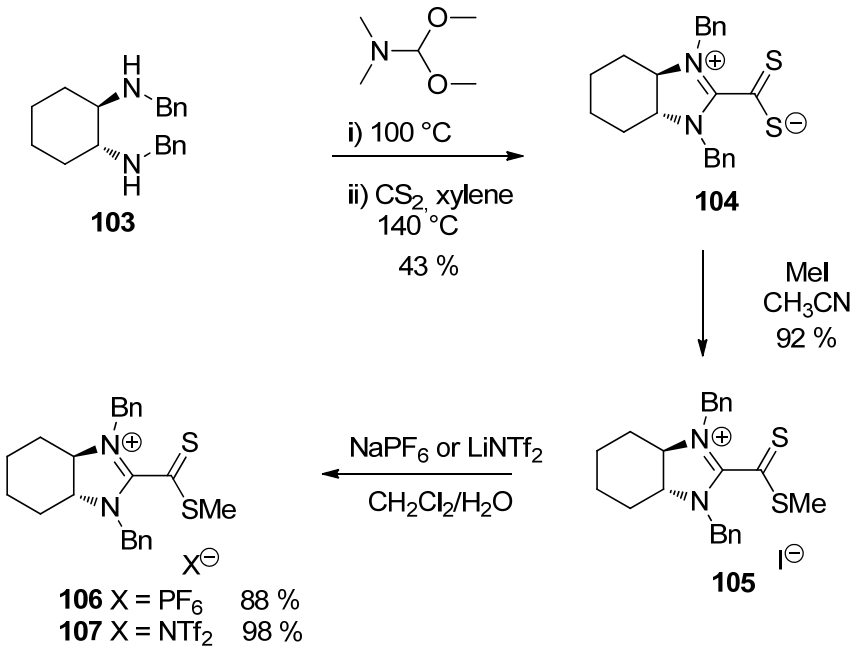


Figure 1. (a) (±)-1-phenyl-2,2,2-trifluoroethanol in toluene-d_8, (b) (±)-1-phenyl-2,2,2-trifluoroethanol (1 equiv.) + **101** (2 equiv.) in toluene-d_8, (c) 1-phenyl-2,2,2-trifluoroethanol (50% *ee*, *S* enriched, 1 equiv.) + **101** (2 equiv.) in toluene-d_8, (d) 1-phenyl-2,2,2-trifluoroethanol (33% *ee*, *S* enriched, 1 equiv.) + **101** (2 eq) in toluene-d_8

For full details see attached copy in the appendix. Winkel, A.; Wilhelm, R. "New Chiral Ionic Liquids Based on Imidazolinium Salts." *Tetrahedron: Asymmetry* **2009,** *20,* 2344-2350.

In addition, a new class of ionic liquid was prepared, based on imidazolinium-dithiocarboxylates (Scheme 32).[318] I was possible to observe in the ^{1}H-NMR a significant rotational barrier between the CS_2Me group and the imidazolinium ring. More important, because of the red color of the cation, due to charge transfer, it was also possible to observe different shifts in the UV/Vis spectra depending on the lipophilicity of the counter anions. In chloroform salt **105** had a maximum at 422 nm, salt **106** at 498 nm and salt **107** at 504 nm. Changing the solvent to methanol resulted for salt **105** in a maximum at 500 nm. Due to their color it is possible to use these salts in order to determine the polarity of solvents and the lipophilic character of anions.[319]



Scheme 32

For full details see attached copy in the appendix. Blanrue, A.; Wilhelm, R. "Methylated Imidazolinium-Dithiocarboxylates: Two Representatives of a New Class of Ionic Liquids." *Synthesis* **2009**, 583-586.

2.5 Carbon Nanomaterials

In order to obtain carbon nanotubes filled with iron based material many literature known procedures were not suitable to obtain material in a significant amount and quality. Therefore, SWCNTs were purchased from Carbon Solutions Inc. and MWCNTs from SunNano and the Mer Corporation. Several purification methods were examined on the carbon nanotubes prepared in the group and on purchased SWCNTs (Carbon Solutions Inc.) and MWCNTs (SUNNANO, MER Corporation). For SWCNTs and MWCNTs most commonly nitric acid treatments was used, which also opened the closed ends of the tubes. Also the oxidant potassium permanganate was used as described by H. Hiura *et al*.[320] Later on, the carbon nanotubes were purified using a multi-step purification method,[321] which was found to be more effective than the procedures used earlier.

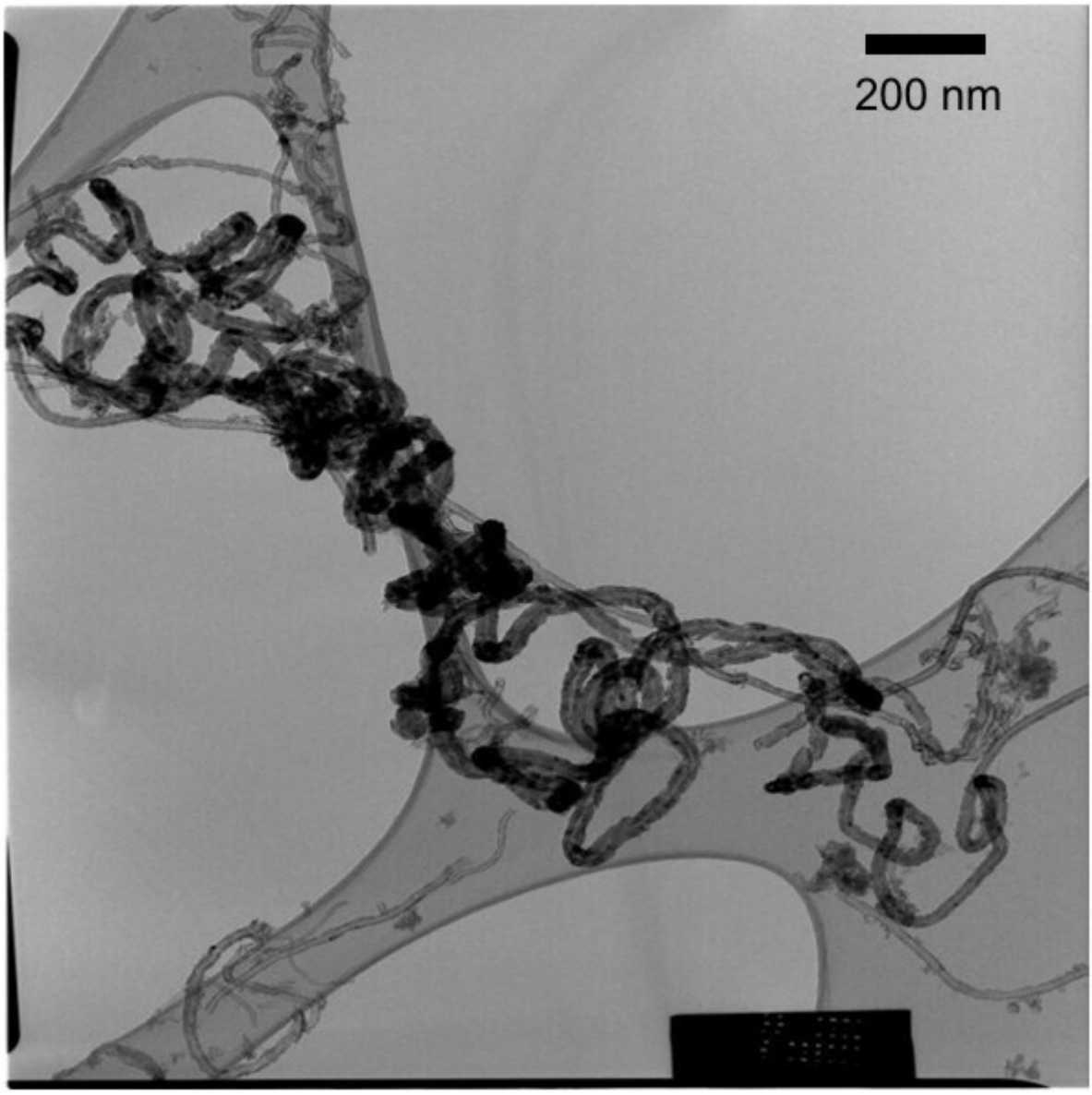


Figure 2. A typical TEM image of purified MWCNTs

For the filling experiments it was focussed exclusively on the aim to obtain α-Fe filled carbon nanotubes. Iron does offer potential advantages over its oxides and other ferromagnetic material due to its higher magnetic moment. In the cases of magnetic separation, where a magnetic field gradient is used to apply a force to the particles, the advantages of a higher magnetization are fairly obvious. The force upon the particle is directly proportional to the magnetization of the particle. In addition, iron has the advantage of being a softer magnet than any of its oxides and other ferromagnetic material, so that it can maintain its superparamagnetism at larger sizes and therefore higher particle moments. At the beginning of the filling experiments, procedures were tried, based on the capillary effect in carbon nanotubes reported originally by Ajayan and Iijima.[322] For such a filling iron salts $Fe(NO_3)_2$ and $FeCl_3$ were used. MWCNTs were suspended in a saturated salt solution in water overnight and then dried in an oven at 80 °C. After further washing with water and ethanol, dried filled tubes were reduced under a stream of hydrogen at 600 °C for 2 h. To an extent it was possible to succeed in filling the nanotubes with α-Fe, though results were not so extraordinary. The level of filling was not as high as often indicated by TEM pictures in the literature with other salt mixtures. Many tubes were not filled. It was found that a high level of filling in nearly all the carbon nanotubes could be achieved before washing the carbon nanotubes, in order to remove salt particles from outside the walls. After the washing the number of filled tubes is far less and also the amount of material in the tubes filled is low. In Figure 3 the pictures show an example of a filled tube.

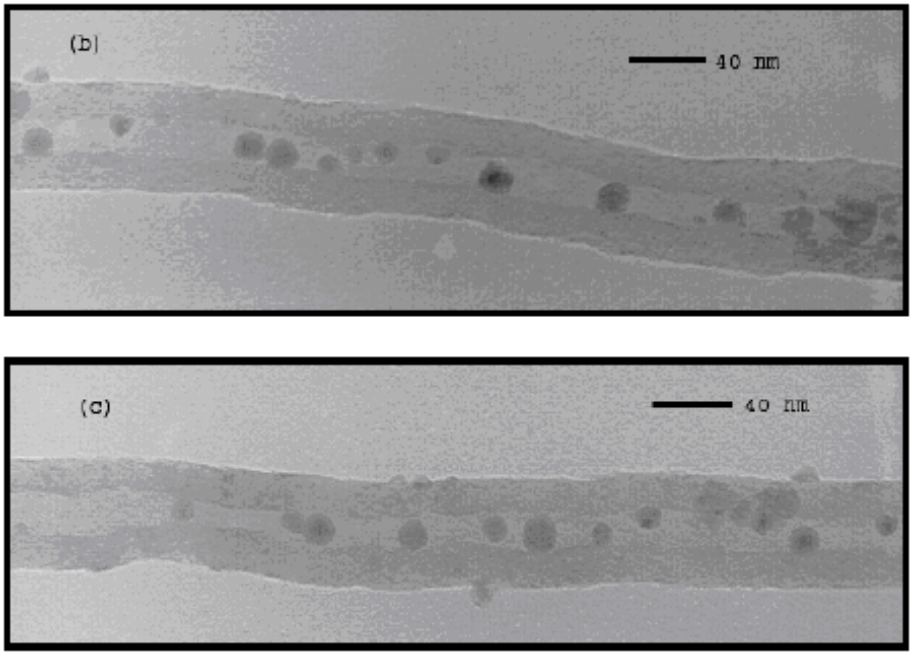


Figure 3. HRTEM images of MWCNTs with α-Fe particles inside through reduction of $Fe(NO_3)_2$

Later on, inspired by the work of Y. Gogotsi *et al*.[221] it was possible to develop a filling procedure for commercially available MWCNTs with a high filling ratio. The tubes were filled with iron oxide nanoparticles from commercially available organic based ferrofluid (EMG 911) (Ferrotec Corporation). These ferrofluids carry magnetite (Fe_3O_4) particles with a characteristic average diameter of 10 nm. MWCNTs used for the experiments were purchased from SES Research (TX, U.S.A.) (formed by arc discharge, avg. dia. 2-20 nm) and Sun Nano (China) (formed by CVD process, avg. dia. 20-70 nm). It was found that the nanoparticles inside the tubes were not carried away during the washing procedure. The iron oxide was reduced with hydrogen to α-Fe (Figure 4).

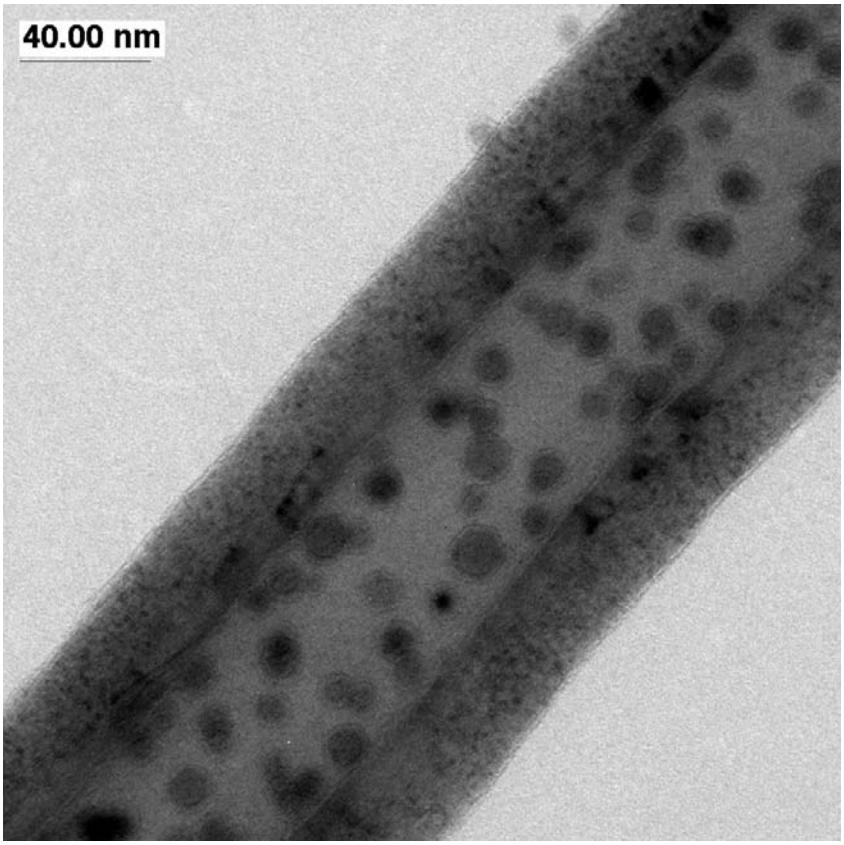


Figure 4. HRTEM image of a MWCNT filled with α-Fe particles through reduction of Fe_2O_3 nanoparticles

For full details see attached copy in the appendix. Jain, D.; Wilhelm, R. "An Easy Way to Produce α-Iron Filled Multiwalled Carbon Nanotubes." *Carbon* **2007**, *45*, 602-606.

Since such a material has high potential in magnetic decantation processes[200-203] and in biological applications[210-213] it was of interest to prepare these structures also directly through the pyrolysis of iron containing complexes. Normally multiwalled carbon nanotubes or

amorphous carbon can be isolated after the pyrolysis of organometallic cobalt complexes under autogenic pressure.[228,229] Therefore, CpFe(arene)PF_6 salts **108** and **109** were prepared and pyrolysed under autogenic pressure, which resulted in different novel carbon nanostructures in remarkable near quantitative yield (Figure 5).[323]

108 **109**

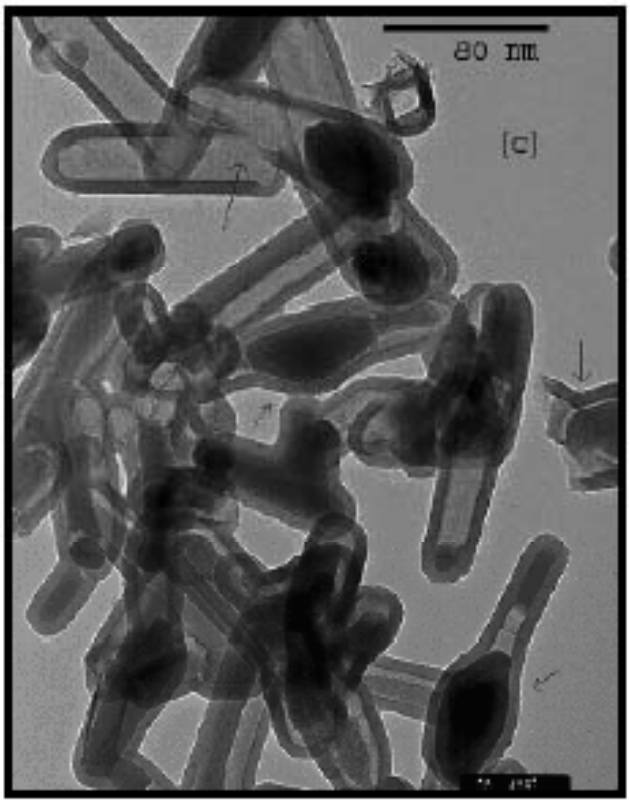


Figure 5. Nanocapsules via pyrolysis from **108**

For full details see attached copy in the appendix. Jain, D.; Winkel, A.; Wilhelm, R. "Solid-State Synthesis of Well Defined Carbon Nanocapsules from Organometallic Precursors." *Small* **2006**, *2*, 752-755.

Since each complex gave different results, further complexes were prepared and pyrolysed in order to determine, if the resulting nanostructure from a certain complex is predictable.[324] Complexes with even only slight differences in their substitution patterns could result in completely different nanostructures. One complex resulted in fibers, which had a diameter

between 35 and 280 nm with a length varying between 3.2 to 10 μm (Figure 6). Nearly all of the fibers had Fe-P nanoparticles incorporated, which were analyzed by EDX. Remarkable is the regular spacing of the particles. The distance between two particles inside a fiber is nearly always the double diameter of the fiber. In most of the cases the diameter of a particle was found to be 80% of the diameter of the fibers, however, sometimes a few particles were found having a diameter larger than the fiber, they were incorporated in.

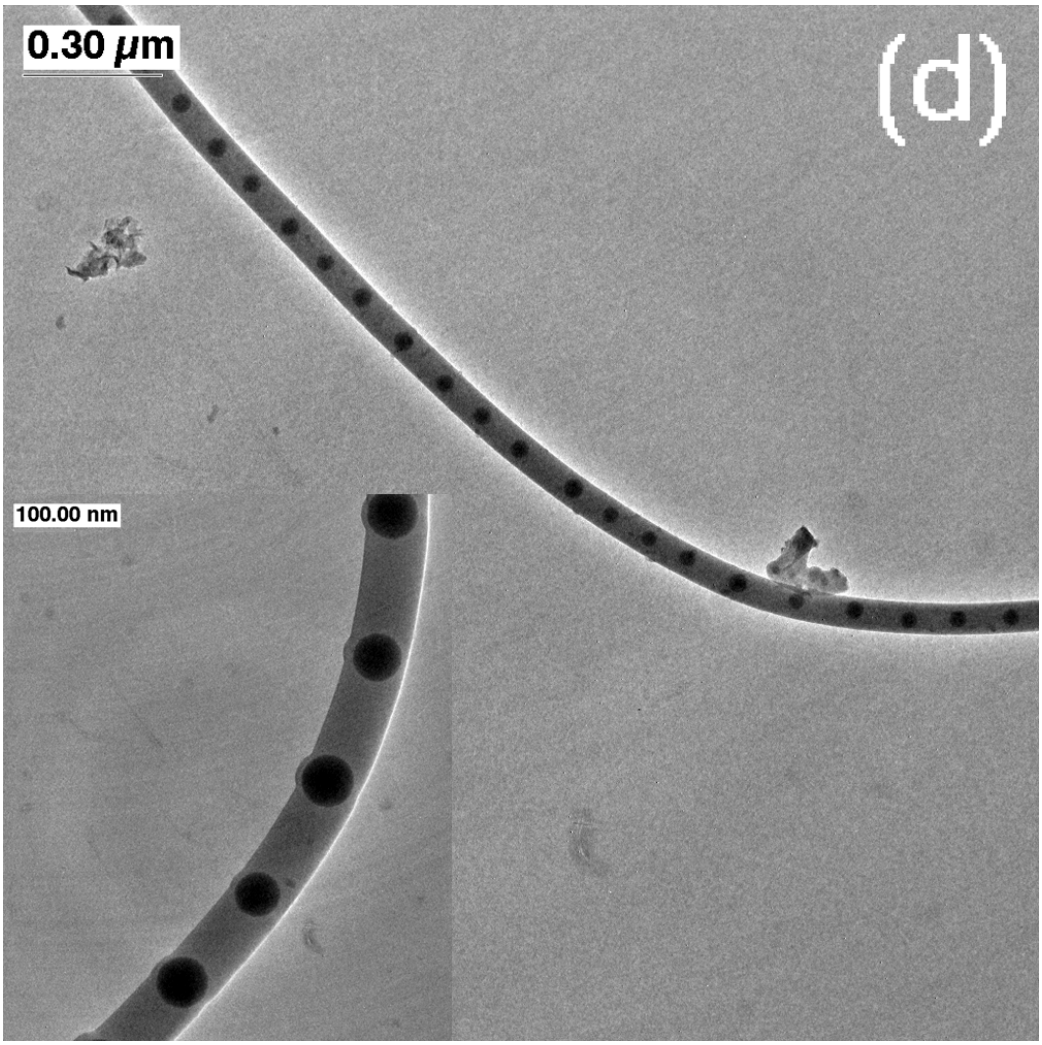


Figure 6. Carbon nanofiber with alternating Fe-P nanoparticles

With another complex circled carbon nanostructures were found, which have been so far only found in meteorites[325] (Figure 7).

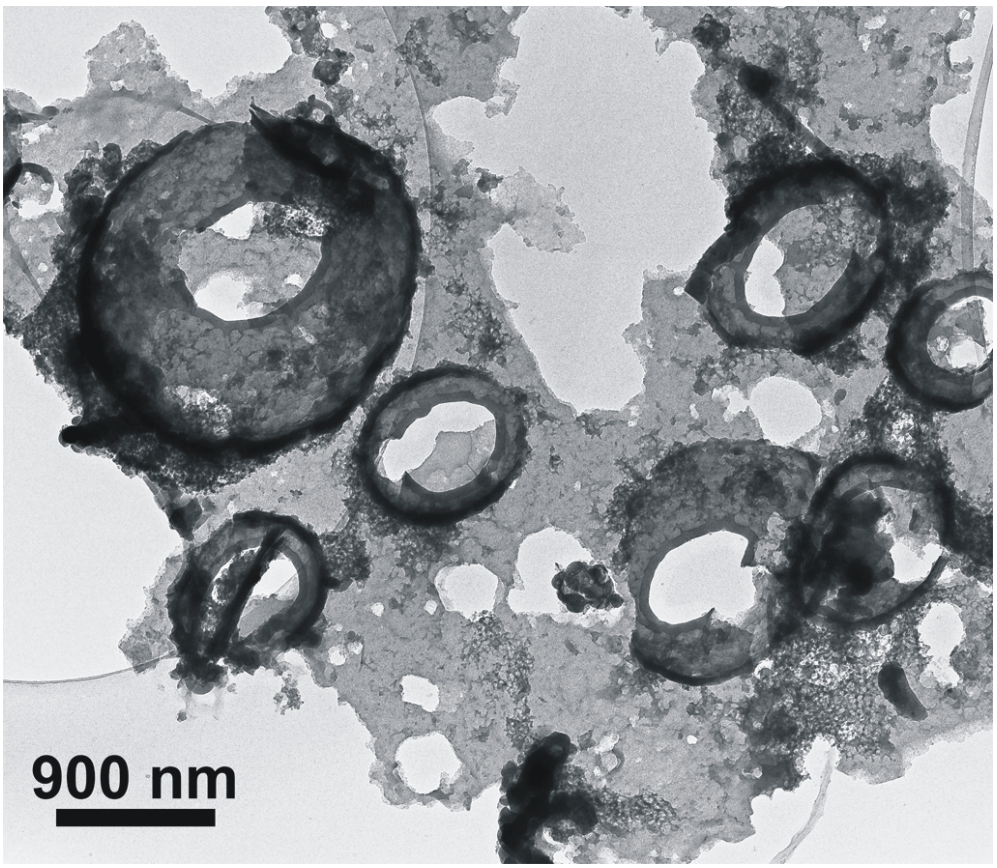


Figure 7. Circular carbon structures from the pyrolysis of a ferrocene derivative

The presented nanostructured material could have for example high potential for gas-storage media,[255,256] Li-intercalation materials for batteries,[257] and cold electron field emitters.[258]

For full details see attached copy in the appendix. Winkel, A.; Jain, D.; Wilhelm, R. "Influence of the Substitution Pattern of Cp-Iron-Arene Salts in the Solid-State Synthesis of New Carbon Nanostructures." *Organometallics* **2008**, *27*, 3430-3434.

Furthermore, oxidized multiwalled carbon nanotubes were found to be soluble in an aqueous urea solution for the first time.[326] First, carbon nanotubes were purified, oxidized and opened. MWCNTs (from SUN Nanotech Co Ltd, produced by CVD) were refluxed in 65% HNO_3 solution for 24 h. The material was filtered and the solid washed with water until the clear washing had a pH of 7. The tubes had a diameter from 20 to 70 nm. IR spectra confirmed the presence of hydroxyl and carboxylic acid groups by the appearance of 1640 cm^{-1} and 3440 cm^{-1} absorption bands in the acid treated samples. The TGA showed a weight loss of 10% showing that COOH groups were present.

In order to study, if the tips of the tubes can be closed with a layer of urea, the functionalized carbon nanotubes were treated with aqueous urea solutions of different concentrations. 100 mg portions of oxidized nanotube samples were dispersed in 20 mL of freshly prepared aqueous urea solutions with concentrations of 3 M, 1.5 M, 0.75 M, 0.375 M, 0.1875 M and 0.075 M, respectively. Directly after the addition, the formation of a CNTs solution was observed. The mixtures were additionally sonicated for 10 min and then left to stir using a magnetic stirrer for 48 h. It was found that the MWCNTs were dissolving in the solutions.

Thereafter, each solution was filtered through a Whatman filter paper. The filtrate was collected and a drop of it was placed on a copper grid coated with holey carbon and the morphology was observed on a transmission electron microscope (TEM). Figure 8 shows that in the solution were MWCNTs. In addition, some amorphous structures attached on some tubes can be seen, which can be attributed to crystalline urea after the evaporation of water.

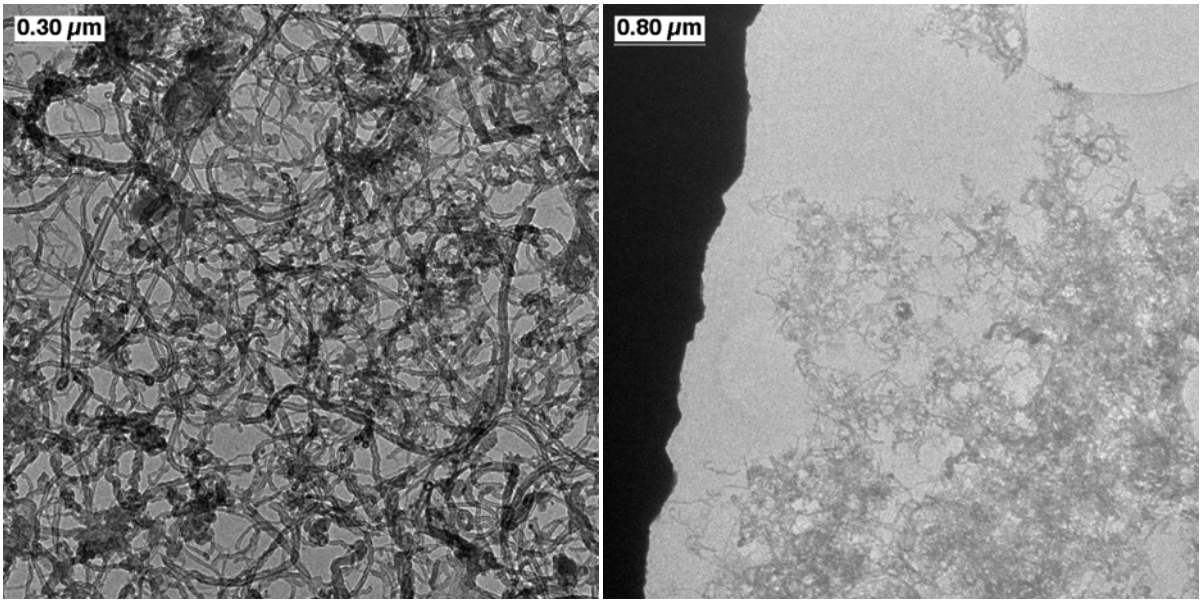


Figure 8. MWCNTs dissolved in urea solution

Next, the amount of dissolved CNTs was calculated by preparing a saturated solution of CNTs and precipitate them by acidifying the solution (Figure 9). Therefore, an excess amount of CNTs (300 mg) was added to 3 mL of 0.075 M urea solution, sonicated for 10 min and then left to stir using a magnetic stirrer for 48 h. Dispersions were then filtered through a Whatman filter paper and the dissolved CNTs were precipitated by adding 3 N HCl. The precipitate was washed thoroughly with deionized water and then dried in an oven at 60 °C for 12 h before measuring the exact mass of CNTs dissolved per mL in the urea solution, which was 11 mg/mL.

It can be assumed that urea molecules are interacting with the hydroxy (–OH) and carboxy (–COOH) groups present on the defect sites of nanotubes by hydrogen bonding. In addition, it is possible that urea, which has a pK_a of 26.9, deprotonates the carboxylic acid functions to form ion pairs, which is responsible for dissolving the nanotubes in water. A control experiment with pristine MWCNTs and a urea solution showed no dissolved CNTs.

In order to redissolve the precipitated tubes, a solution of Na_2CO_3 was added to the CNTs, however, they were not dissolving. Therefore, a solution of Na_2CO_3 was added to a urea solution with CNTs and it was found that the tubes were also precipitating from the solution (Figure 9).

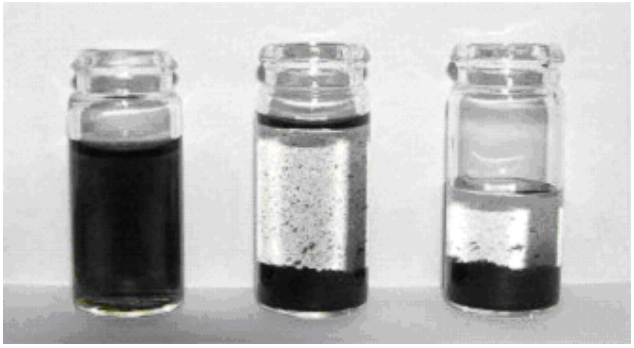


Figure 9. (from left to right) a filtered solution of CNTs with urea, after addition of 3N HCl, after addition of sat. $Na_2CO_{3(aq)}$

In order to investigate, if this was due to a salting out effect, NaCl solution was added to a urea solution of CNTs and it was also found that the tubes immediately precipitate from the solution. The same effect was found, when saturated solutions of $NaBF_4$, NH_4Cl, and CsCl were added. When solutions of NaOAc, Na_2SO_4, NH_4OAc, or $CsNO_3$ were added, it was also found that the tubes were precipitating; however, it took up to 16 h until a clear solution with a precipitate was formed. When Et_3N was added to the CNT solution, no change was observed. It can be assumed that the increase of concentration of cations cause the aggregation of the carbon nanotubes.

In addition, also SWCNTs were oxidized and, after washing with water, treated with a 0.075 M solution of urea. After filtering and precipitation with 3 N HCl and washing with water, it was found that a saturated solution contained 3.8 mg/mL SWCNTs.

2.6 Conclusion

During this work it was possible to contribute to the field of metal free Lewis acids in synthesis, focusing already from the very beginning on asymmetric catalytic examples. Metal-free Lewis acids can be categorized as part of the research area of non-covalent organocatalysis. The desired Lewis acids, e.g. resonance stabilized carbocations, can be readily prepared in only a few steps and on a large scale from cheap starting materials and structural and electronic features can be easily modified. The catalysts were applied in synthetic important reactions and were even suitable to activate thiocarbonyl groups and thiiranes.

Furthermore, imidazolinium-dithiocarboxylate inner salts were introduced as novel organocatalysts in asymmetric catalysis. The chiral catalysts were applied in a range of synthetic important asymmetric reactions to prepare enantiopure compounds. It was shown that the imidazolinium moiety has a weak Lewis acidity and the dithiocarboxylate group is a Lewis base moiety. In case of the Staudinger reaction excellent yields and *ee*`s were obtained.

Moreover, imidazolinium salts with hydrogen at the C-2 position can be transferred into carbenes with a base and used as Lewis base catalysts. A structural and conceptual novel camphor based carbene was developed giving excellent *ee´*s in the Wynberg reaction. It was also possible to show for the first time that hindered Brønsted bases can act as Lewis base catalysts, which was utilized in the Staudinger and Wynberg reaction. Also new chiral carbene ligands, which are incorporating one or two hydroxy groups, were developed. These new bidentate and tridentate ligands were prepared in a few steps on large scale and were investigated in catalysis with a range of metals, like zinc, copper, nickel, iron and titanium. In addition, the application of the new ligands with large silyl groups gave good results in cross-couplings.

Next, new chiral and achiral ionic liquids, which are stable in the presence of strong bases, based on imidazolinium cations were prepared. The new ionic liquids incorporated also ligator atoms, which made it possible to apply these new liquids in reactions involving Grignard reagents. The asymmetric addition of Grignard reagents to aldehydes was investigated in the beginning. In addition, the new liquids were suitable chiral NMR-shift reagents.

Finally, a new method was developed to prepare iron filled CNTs on larger scale. CNTs containing ferromagnetic material have high potential in many processes. The advantage would be to recover these NTs with magnets, which would be of high interest in industrial processes. If drugs are attached to the tubes, it would be possible to deliver those directly to the desired place in the body *via* magnetic fields. Moreover, in order to prepare filled tubes *in situ*, organometallic complexes based in CpFe(arene) salts were pyrolysed in order to obtain not only carbon nanotubes but also novel nanostructures based on carbon. Different metal complexes resulted in different nanostructures of carbon, like carbon nanotubes, fibers and other forms. The pyrolytic, solid state synthesis to nanomaterials from organometallic molecules of defined composition and morphology provides a unique alternative entry into the field of nanomaterials, which allows control of elemental ratios and tailoring.

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4. Appendix

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Lewis Acid Organocatalysts

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Lewis acid catalysts are generally referred to metal salts like aluminium chloride, titanium chloride, zinc chloride and other metal salts. Their application in asymmetric catalysis can be achieved by the addition of enantiopure ligands to these salts. However, not only metal centers can function as Lewis acids. Compounds containing carbenium, silyl or phosphonium cations display Lewis acid catalytic activity. In addition, hypervalent compounds based on phosphorus and silicon, inherit Lewis acidity. Furthermore, ionic liquids, organic salts with a melting point below 100 °C, have revealed the ability to catalyze a range of reactions either in substoichiometric amount or, if used as the reaction medium, in stoichiometric or even larger quantities. The ionic liquids can be often efficiently recovered. The catalytic activity of the ionic liquid is explained by the Lewis acidic nature of their cations. This review covers the survey of known classes of metal-free Lewis acids and their application in catalysis.

Contents

1 Introduction

Until recently the most popular method in asymmetric catalysis was the application of metal complexes. This is not surprising, since the use of different metals, ligands and oxidation states makes it possible to tune selectivity and asymmetric induction very easily. Thus, the concept of asymmetric catalysis has

become almost synonymous with the use of metals coordinated by chiral ligands.[1, 2] In many examples the metal is a Lewis acid.[3]

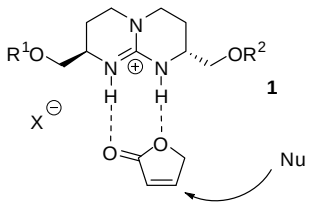
Roles that are normally associated with metals as Lewis acids and as redox agents,[4, 5] can be emulated by organic compounds. This review will introduce the reader to the research field of Lewis acid organocatalysts. This field, compared to other types of organocatalyst, which are highlighted in the other articles of this issue, is still limited. The number of asymmetric catalyzed examples is small, and the obtained enantiomeric excess is sometimes low. Therefore, this review will also cover a number of reactions promoted by achiral catalysts. Nevertheless, due to the broad variety of possible reactions, which are catalyzed by Lewis acids, this research field possesses a large potential.

Compounds containing carbenium, silyl or phosphonium cations can act as Lewis acids. In addition, phosphorus and silicon based hypervalent compounds display a Lewis acid catalytic activity. Furthermore, ionic liquids, organic salts with a melting point below 100 °C, have shown the ability to catalyze a group of reactions either in substoichiometric amount or, if used as the reaction medium, in stoichiometric or even larger quantities. The solvents can be efficiently recovered after the reaction. Each type of these compounds will be presented in a separate section.

This review will concentrate on metal-free Lewis acids, which incorporate a Lewis acidic cation or a hypervalent center. Lewis acids are considered to be species with a vacant orbital.[6, 7] Nevertheless, there are two successful classes of organocatalysts, which may be referred to the Lewis acids and are presented in other articles of this issue. The first type is the proton of a Brønsted acid catalyst, which is the simplest Lewis acid. The obtained enantioselectivities are due to the formation of a chiral ion pair. The other type are hydrogen bond activating organocatalysts, which can be considered to be Lewis acids or pseudo-Lewis acids.

There are some types of organic cations which cannot be placed under the headline of Lewis acid organocatalysts. For example, one type is the chiral

guanidinium salt **1** which has been used as a catalyst[8] in the Michael reaction. Due to the mode of activation as shown in Scheme 1, this salt belongs to the hydrogen bond activating organocatalysts. In this example, **1** gave only racemic product (Scheme 1). In addition, a chiral amidinium salt,[9] which catalyzed the Diels-Alder reaction with significant enantiomeric excess, would belong also to the class of hydrogen bond activating organocatalysts.



Scheme 1

Another type would be ammonium cations of the types RNH_3^+, $R_2NH_2^+$ or R_3NH^+ which could be considered to be Brønsted acids or hydrogen bond activating organocatalysts. Fully substituted ammonium cations, R_4N^+, could interact with a carbonyl group lowering the electron density of its carbon atom. Yet, since the ammonium cation does not possess an empty orbital to take up an electron pair, it is not a Lewis acid. However, enantiopure ammonium salts have been used very efficiently in asymmetric phase transfer catalysis, which has been reviewed.[10-19]

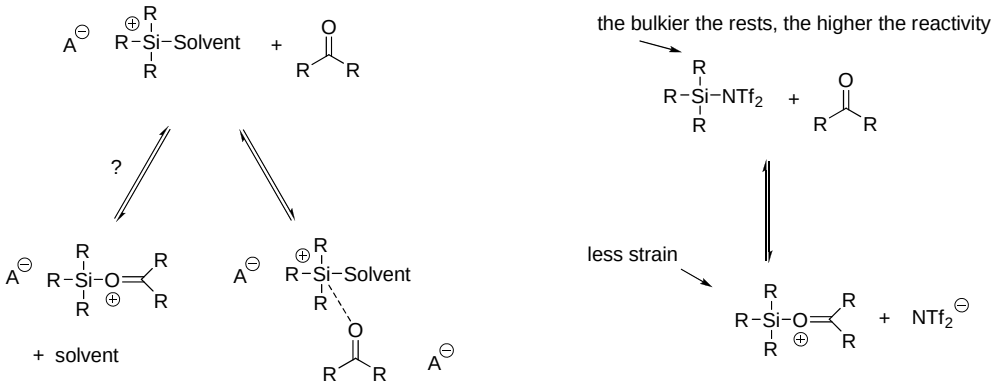
One section in this review will deal with silyl cations, another one with hypervalent silicon compounds. The concept of hypervalent silicon compounds belongs strictly speaking to the class of Lewis base catalysis. However, since a Lewis base forms in situ with silicon containing reagent or $SiCl_4$ an intermediate, which functions as a Lewis acid to activate substrates during the reaction, we would present also a few examples in this review. Since silicon is a semimetal we leave it up to the reader to decide whether silicon catalysts should be considered as organocatalysts.

Another semimetal is boron, which has been used for a long time as Lewis acid, e.g. BF_3, and of which enantiopure derivatives have been applied very successfully. Asymmetric boron catalysts have been reviewed[20-23] and will not be a part of this article.

2 Silyl Cation Based Catalysts

Silicon based Lewis acids are known for some time, which chemistry in catalysis has recently been reviewed.[24] Most examples in the literature are mainly based on achiral species and will be presented in this section only briefly. In general, a broad variety of reactions can be catalyzed with compounds like Me_3SiOTf, Me_3SiNTf_2 or Me_3SiClO_4. One advantage over some metal Lewis acids is that they are compatible with many carbon nucleophiles like silyl enol ethers, allyl organometallic reagents and cuprates.

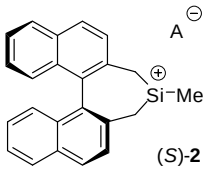
Overall, it is possible to divide the silyl Lewis acids into two groups, depending how strong the counter anion interacts with the silicon atom as shown in Scheme 2. In case a very weakly coordinating anion is part of the compound, one could consider that a free silyl cation is present. However, the silyl cation is very strong and will be coordinated by solvent molecules, like acetonitrile or toluene.[25, 26] This complex could activate, for example, a carbonyl group. Whether the carbonyl group replaces the solvent molecule, is not known. In case a more coordinating anion is present, a neutral silicon molecule should be postulated. A carbonyl oxygen could perform an exchange with the $[NTf_2]$ ligand. The bulkier the three alkyl rests around the silicon atom are, the better the exchange takes place, due to the release of strain, replacing the larger $[NTf_2]$ substituent with a smaller carbonyl ligand.[27-29]



A: weakly coordinating anion e.g. $B(C_6F_5)_4$

Scheme 2

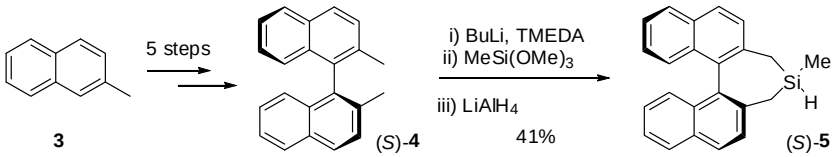
In 1998 the groups of Jørgensen and Helmchen reported the preparation of the chiral silyl cationic salt **2** (Scheme 3).[30] This was the first time that a chiral silyl cation was used as a catalyst in an enantioselective reaction. In order to ensure that the silyl salt had a high reactivity, the almost chemically inert and non-coordinating anions tetrakis[pentafluorophenyl]borate [TPFPB] and tetrakis[3,5-bis(trifluoromethyl)phenyl]borate [TFPB] were chosen as counter anions.



a A = TPFPB
b A = TFPB

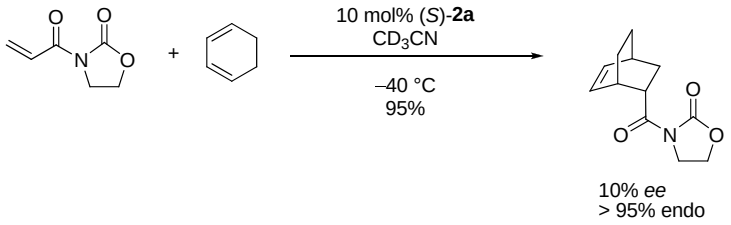
Scheme 3

The salt precursor was prepared according to the following route as shown in Scheme 4. The desired enantiopure binaphthyl compound (*S*)-**4** was made from 2-methylnaphtalene (**3**) over 5 steps, which included also a resolution step.[31-33] The final precursor (*S*)-**5** was obtained in 41% yield via a deprotonation of (*S*)-**4** followed by the reaction with methyltrimethoxysilane and a subsequent reduction.



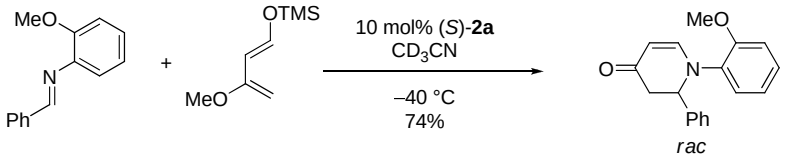
Scheme 4

Since silyl cations are highly reactive and moisture sensitive, the salts (*S*)-**2a** and (*S*)-**2b** were prepared in situ from the air and moisture stable precursor (*S*)-**5** via a hydride transfer[34, 35] with trityl tetrakis[3,5-bis(trifluoromethyl)phenyl]borate [Tr][TFPB] or trityl tetrakis[pentafluorophenyl]borate [Tr][TPFPB]. The authors showed by ^{29}Si-NMR studies that the desired salts were formed. The silyl salt (*S*)-**2a** was then tested in the Diels-Alder reaction as shown in Scheme 5. A good reactivity was found, and the product was obtained in 95% yield with higher than 95% *endo* selectivity at –40 °C in 1 h. However, only 10% *ee* was achieved.



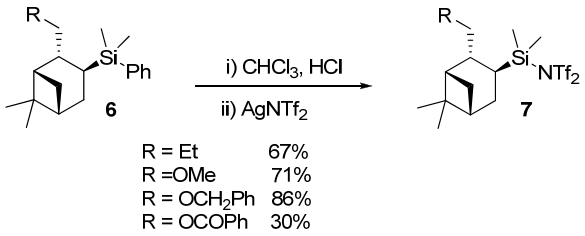
Scheme 5

In addition, it was possible to show that salt (*S*)-**2a** could catalyze the aza-Diels-Alder reaction as presented in Scheme 6. Benzylidene-2-methoxyaniline and Danishefsky´s diene in the presence of 10 mol% catalyst at –40 °C gave the desired product in 74% yield in just 2 h. Unfortunately, the obtained product was racemic.



Scheme 6

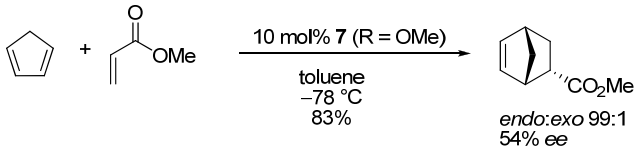
A second example of an enantiopure silicon based catalyst was reported by the group of Ghosez.[27] They concluded from the results of Simchen and Jonas[28] as described above, that R_3SiNTf_2 compounds, bearing bulky chiral groups, should possess a good catalytic activity. Silylated sulfonimides from readily available (–)-myrtenal were obtained in few steps to give the desired precursors **6** shown in Scheme 7. The salts were prepared in situ by transforming silane **6** to the corresponding silyl chloride with HCl in $CHCl_3$ followed by the treatment with $AgNTf_2$.



Scheme 7

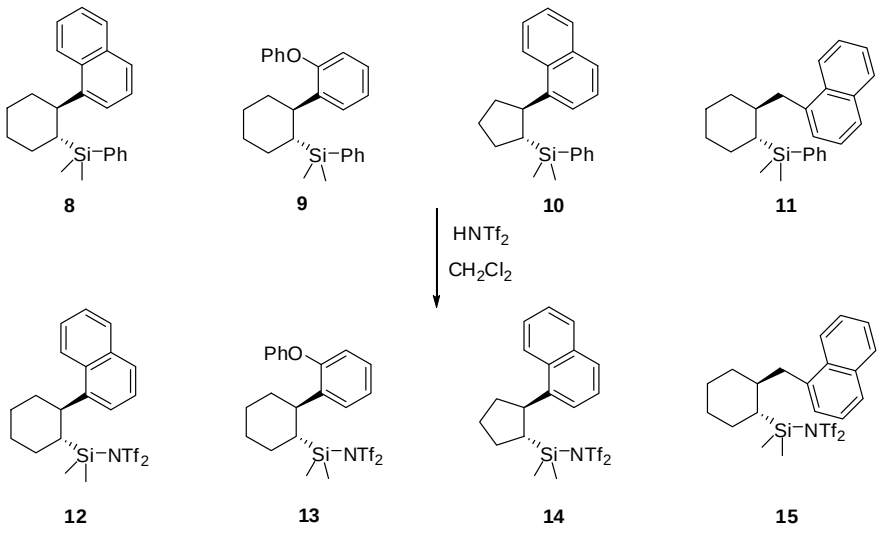
The catalysts were tested in the Diels-Alder reaction of cyclopentadiene and methyl acrylate. The best result is given in Scheme 8. Catalyst **7** (R = OMe),

bearing an oxygen atom, which can stabilize the silicon center through coordination, gave the product in 83% yield with an *ee* of 54% in favour of the *endo* product in 1.5 h. In case of **7** (R = Et) without an oxygen atom, a significantly lower *ee* of 7 % was observed. Next to toluene, solvents like ether, propionitrile or CH_2Cl_2 were tested, but gave no desired product.



Scheme 8

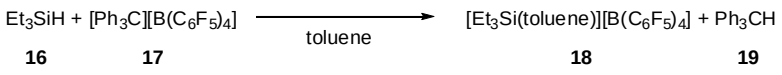
The same group reported the synthesis of enantiopure cycloalkylsilyl triflimides.[36] Some examples are presented in Scheme 9. The precursors were prepared from cyclohexenones and cyclopentanones, which were transferred in three steps into racemic 2-aryl- and arylmethyl-3-dialkylphenylsilyl cycloalkanones. These were resolved by preparative chiral HPLC. Next, the carbonyl function was removed to give the desired precursors to the silyl triflimides. The latter were obtained in situ directly by the treatment with $HNTf_2$. The formation of these compounds could be followed by ^{1}H-NMR due to the signals of the methyl groups connected to the silicon atom. The signals shifted from 0.20 ppm to 0.60 ppm. In addition a signal at 7.36 ppm appeared due to the formation of benzene during the course of the reaction.



Scheme 9

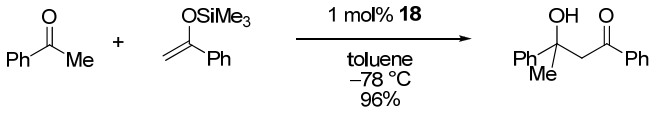
The salts were afterwards tested in the Diels-Alder reaction of methyl acrylate and cyclopentadiene as depicted above in Scheme 8. In contrast to the previous investigation,[27] CH_2Cl_2 was found to be a good solvent for the reactions. 10 mol% Catalyst was prepared in situ, and the reaction was performed at −78 °C in the presence of 2,6-di-*tert*-butyl-4-methylpyridine to trap any residual $HNTf_2$. The best result was obtained with compound **12** giving the product in high *endo* selectivity in 96% yield and 50% *ee*. When −100 °C was chosen as the reaction temperature, 94% yield and 59% *ee* were reached in less than 2 h. Contrary to the previous example, catalyst **13** containing an oxygen atom, gave poor results with low *endo* selectivity and 35% *ee*. The cyclopentane based analogue **14** gave an *ee* of 56%; however, the *endo*/*exo* selectivity was 32%. The results with catalyst **15** showed that an insertion of a methylene group between the cyclohexene ring and the 1-naphthyl group gave a significant lower *ee* of 7% due to the higher conformational mobility in this catalyst.

Further on, Sawamura et al.[37] investigated the influence of different counter anions on the catalytic activity of cationic silicon Lewis acids. In the studies an achiral salt was used. In previous cases[30] acetonitrile was used as a solvent, which is known strongly to coordinate the silicon cation species. Therefore, the application of toluene as a solvent was investigated with a silicon cationic species. Although even toluene is coordinating a silicon cation,[25, 38] an enhanced activity compared to other solvents, was found. The achiral salt was prepared in situ from triethylsilane and $[Ph_3C][B(C_6F_5)_4]$ (**17**) as depicted in Scheme 10.



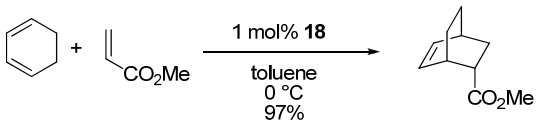
Scheme 10

The salt **18** was explored in the Mukaiyama aldol reaction with acetophenone, and a yield of 96% was obtained after 1 h at −78 °C (Scheme 11). When Me_3SiOTf was used as a catalyst, a yield of 0% was observed. Me_3SiNTf_2 and Et_3SiNTf_2 resulted in 12 and 8 % yield, respectively.



Scheme 11

In addition, the Diels-Alder reaction was found to be catalyzed by salt **18** giving the *endo*-product in 97% yield in 1 h. Application of Me_3SiOTf resulted in no product formation, while Me_3SiNTf_2 and Et_3SiNTf_2 gave a yield of 6 and 13%, respectively. Both reactions proceeded in the same way in the presence of the proton scavenger 2,6-di-*tert*-butylpyridine with salt **18**, which should rule out a proton promoted reaction.

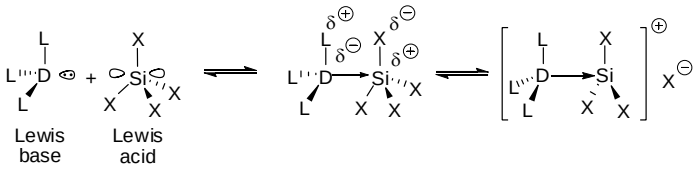


Scheme 12

In summary, due to the low *ee´*s so far obtained with silyl based Lewis acids there is still much room for optimization. The latter is a promising and worthwhile task, considering the large number of reactions catalyzed by the achiral analogues and their advantages over metal Lewis acids.

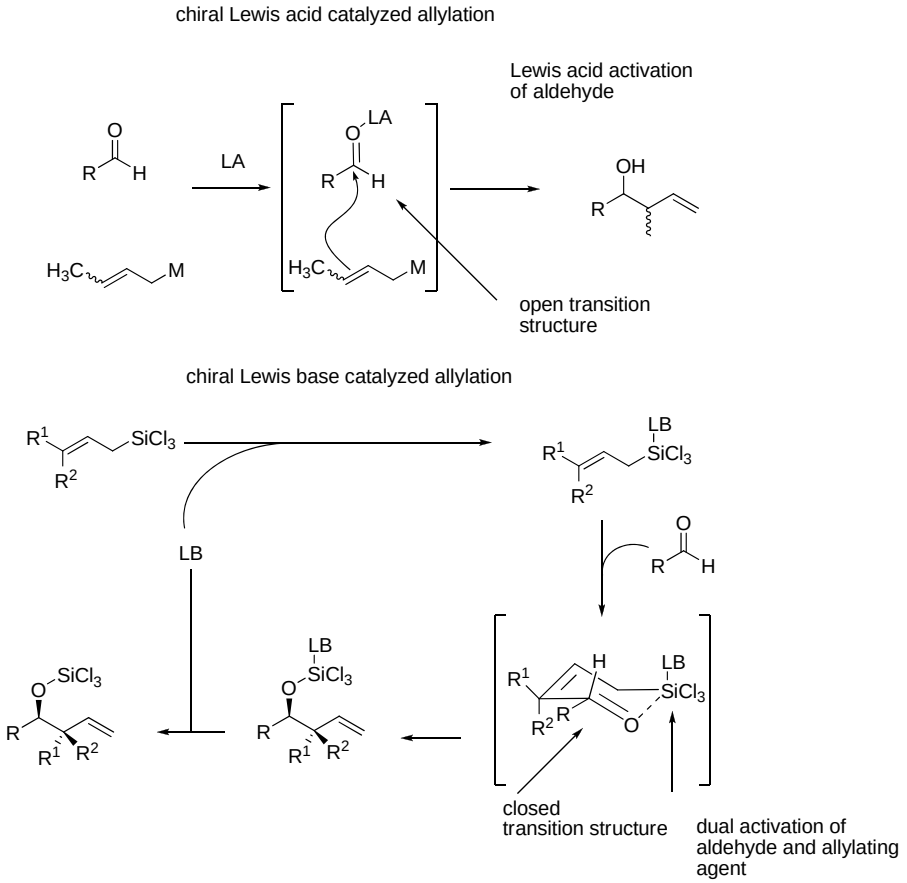
3 Hypervalent Silicon Based Catalysts

Lewis bases in combination with silicon containing reagents can form in situ a Lewis acid center, which can activate a substrate. Therefore, a few examples would be presented in this section, although this type of catalysis is mainly considered to be part of Lewis base catalysis. Due to the valence shell expansion capability of silicon, Lewis bases tend to interact with vacant orbitals residing on the silicon. This interaction of Lewis bases increases the electron density on the most labile ligand of the silicon atom. Once the ligand is ionized or partially ionized, a positively charged silicon complex is formed, which acts as a Lewis acid due to its free 3d-orbitals responsible for many organic transformations[24, 39-44] (Scheme 13).



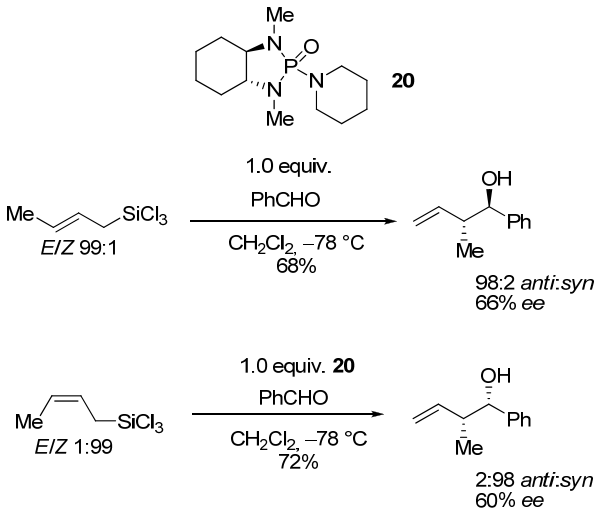
Scheme 13

First, a few examples with silicon atom in one of the reaction partners will be discussed. The asymmetric allylation of carbonyl compounds with an allylating agent leads to homoallylic alcohols with two consecutive stereocenters along with a carbon-carbon bond formation. The traditional method for this is the use of Lewis acids that activate an electrophilic aldehyde towards nucleophilic attack of an allyl metal reagent (Scheme 14).[2] The use of the latter gives high enantioselectivity, but lacks diastereoselectivity. This is because of the non-rigid transition state in the reaction. In contrast, chiral Lewis base catalyzed allylations provide a dual mechanism of activation, which involves binding of the Lewis base with a nucleophile (trichlorosilane), thus generating a reactive hypercoordinated silicate species, which further coordinates with aldehydes. Since the reactions proceed in the close assembly of allyltrichlorosilane, aldehyde and chiral Lewis base, a high degree of diastereoselectivity and enantioselectivity can be achieved.[40]



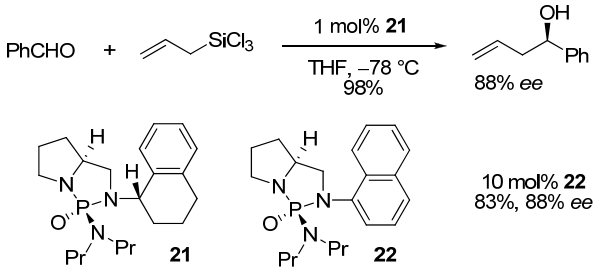
Scheme 14

The first example of a chiral Lewis base promoted allylation was given by Denmark and coworkers in 1994.[45] Stoichiometric amounts of chiral phosphoramide (*R*,*R*)-**20** facilitated the enantioselective allylation (Scheme 15). There was a complete stereochemical correlation between the geometry (*E*/*Z*) of allylsilane and the diastereomeric ratio (*syn*/*anti*) of the products.



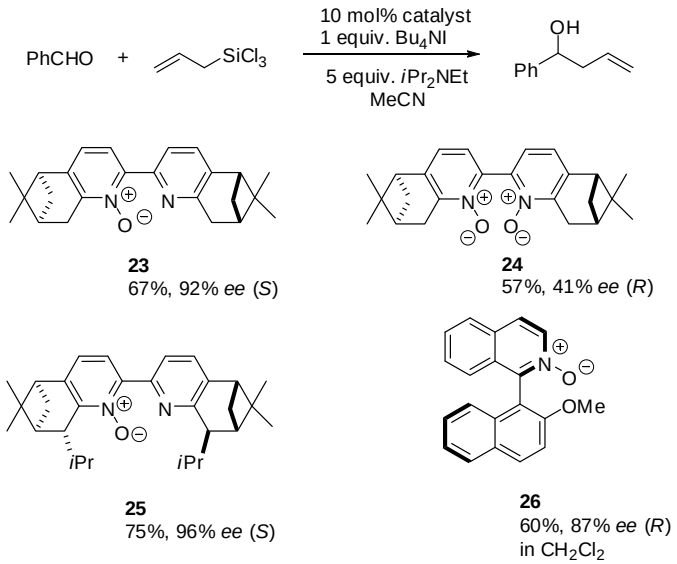
Scheme 15

Similar results were reported by the Barret group by using stoichiometric amounts of an enantiopure 2-(2-pyridinyl)-2-oxazoline.[46] In 1996, Iseki and Kobayashi achieved a catalytic version of the asymmetric allylation.[47] They applied proline based chiral HMPA derivatives for the allylation. The catalyst **21** proved to be the best one regarding catalyst loading down to 1 mol% (Scheme 16).[48]



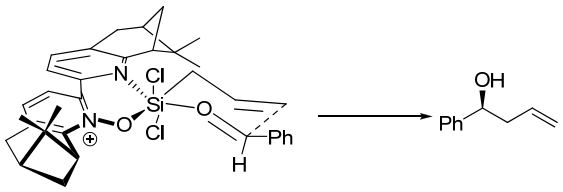
Scheme 16

Amine *N*-oxides, possessing the property of Lewis basicity, have also been exploited in an enantioselective allylation. Malkov and Koĉovsky prepared a series of chiral *N*-oxide catalysts and found, that ligands **23** and **25** afforded good yield and stereoselectivity (Scheme 17).[49-51]



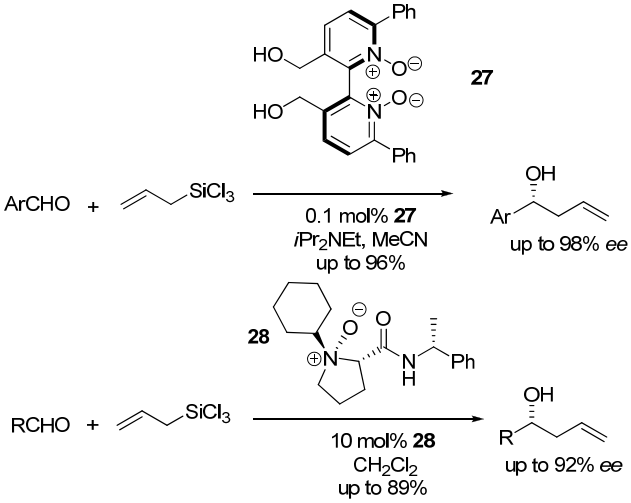
Scheme 17

Mechanistic analysis suggests that the *N*-oxide activates the trichlorosilane functionality and the other nitrogen atom stabilizes the complex by chelation, thus leading to closed chair-like transition state.[49, 52] Scheme 18 shows the possible transition state.



Scheme 18

Hayashi et al. achieved high catalytic activity by using axially chiral *N*-oxide catalyst **27**. As compared to other organic catalysts, the reaction proceeded much faster, and high enantioselectivities were obtained with 0.01 to 0.1 mol% catalyst loading.[53-55] In 2005, Hoveyda and Snapper used a novel proline based aliphatic *N*-oxide **28** for an asymmetric allylation (Scheme 19).[56]

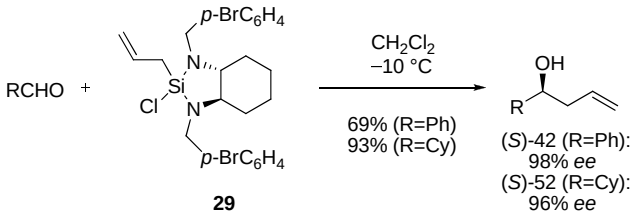


Scheme 19

In addition, Iseki et al. reported a highly enantioselective allylation reaction with aliphatic and unconjugated aldehydes. They used chiral DMF derivatives and observed a dramatic increase in the yield and enantioselectivity of the reaction, when a stoichiometric amount of HMPA was employed.[57, 58]

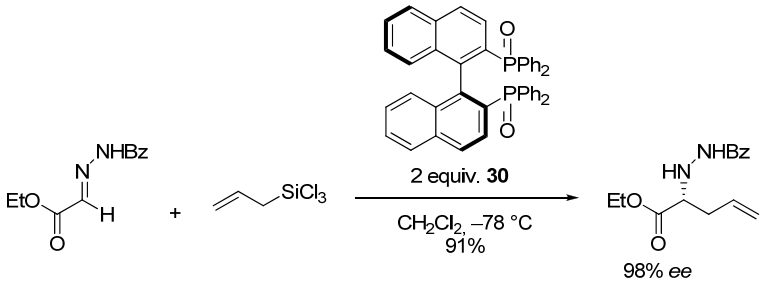
Next, enantiopure silicon allylation reagent will be presented, which already inherits Lewis acidity. It is accepted that Lewis acidity of silicon, as well as its high tendency to expand valence shell increases,[59, 60] if it is tetravalent and incorporated into strained 4- or 5-membered ring systems (strain-release Lewis acidity).[61] This corresponds to smaller energy gaps between sp^3 and dsp^3 orbitals of a strained system as compared to an acyclic species.

Leighton has combined this concept of *strained silacycles*[62-66] with the asymmetric allylation chemistry in a series of publications.[60, 67-70] Leighton`s allylic silacyclopentane **29**[67] (Scheme 20) equally works for allylation of aromatic and aliphatic aldehydes in the absence of additional Lewis bases (promoter activator) or Lewis acids with high yield and enantioselectivity. The mechanism of the reaction is not completely understood, but it likely involves a cyclic transition state with a trigonal bipyramidal geometry at a pentacoordinated silicon.[59, 70]



Scheme 20

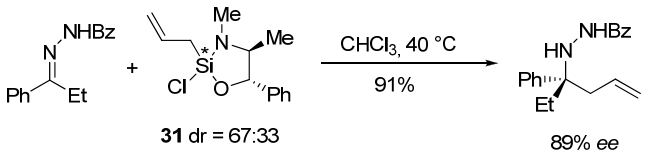
Furthermore, next to aldehydes, acylhydrazones have been used in the allylation reaction. Kobayashi and coworkers found that achiral phosphineoxides catalyze the allylation of acylhydrazone.[71, 72] Next, a method for an asymmetric allylation of *N*-acylhydrazone with chiral BINAP dioxide **30** was developed (Scheme 21).[71, 72]



Scheme 21

The synthesis of tertiary carbinamines is an important goal in organic synthesis. Leighton reported allylation of benzoylhydrazone by using the allylic silane reagent **31** giving tertiary carbinamines with high enantioselectivity in 24 h (Scheme 22).[70] This reaction is exceptional, since high enantioselectivity was achieved with the diastereomeric mixture of the allylating reagent **31**. There may be two possible explanations.[60] First, by using 1.5 equiv. excess of **31**, only the

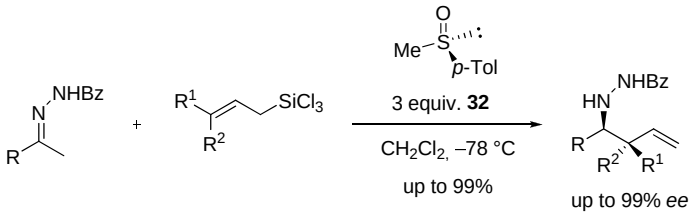
major diastereomer transfers an allyl group and the minor remains unreactive. Second, the reaction proceeds through a hypervalent silicon intermediate, which is prone to a pseudorotational process. More likely the stereogenic silicon fast epimerizes and only one diastereomeric intermediate transfers the allyl group.



Scheme 22

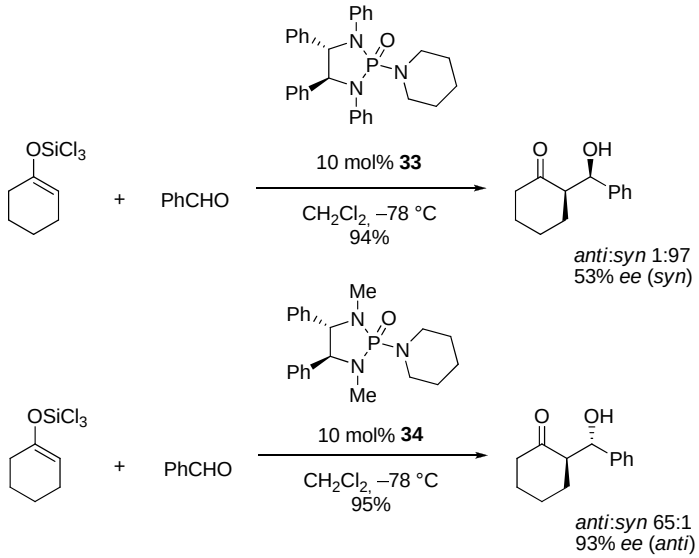
Imidazoles/benzimidazoles and chiral carbinamines are of particular importance.[73, 74] Recently, Leighton et al. developed a method for enantioselective imidazole directed allylation of aldimines and ketimines[75] with an analogue of **31**.

Next to P(O) or N(O) Lewis bases, there are very rare cases where enantiopure sulfoxides are used in combination with silanes. Kobayashi and coworkers reported a highly diastereoselective and enantioselective allylation of hydrazones with chiral sulfoxide **32** (Scheme 23).[76] Massa[77, 78] and Barness[79] reported the asymmetric allylation of aldehydes with enantiopure sulfoxides, respectively, with moderate selectivity.



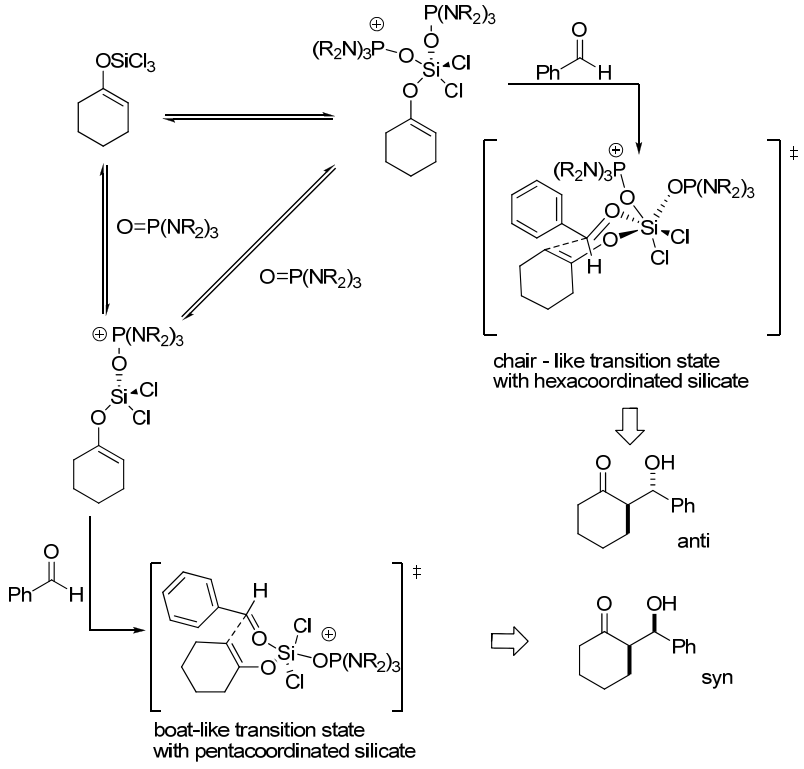
Scheme 23

In the following a few examples of the asymmetric aldol reaction are given. Silyl enol ethers (O-Si) resemble very much allylsilanes (C-Si) in terms of structure and mode of action. That is why Lewis base catalyzed aldol reactions of silyl enol ethers have been extensively studied. The first example of Lewis base catalyzed asymmetric aldol reaction of trichlorosilyl enol ether with chiral phosphoramide[80-91] was reported by Denmark et al. (Scheme 24).



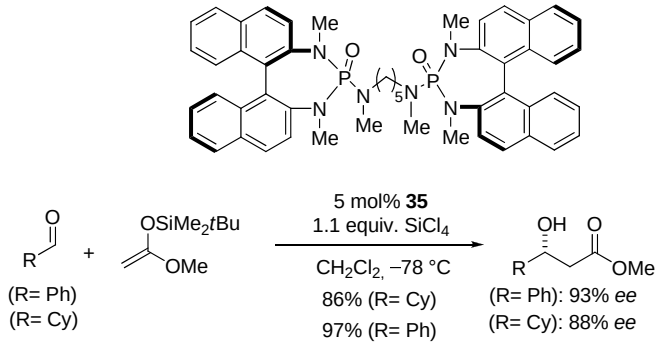
Scheme 24

The coordination state of the silyl enol ether in the transition state strongly influences the diastereoselectivity (*syn*/*anti*). If a ligand is sterically demanding, like phosphoramide **33**, a boat-like transition state with a pentacoordinated silicate is formed and affords the *syn* product in the reaction of trichlorosilyl enol ether with benzaldehyde. In contrast, the less hindered ligand **34** gave the *anti* product through a chair-like transition state with a hexacoordinated silicate (Scheme 25).



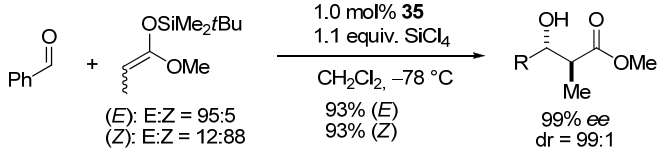
Scheme 25

Denmark utilized chiral base promoted hypervalent silicon Lewis acids for several highly enantioselective carbon-carbon bond forming reactions.[92-98] In these reactions, a stoichiometric quantity of silicon tetrachloride as achiral weak Lewis acid component and only catalytic amount of chiral Lewis base were used. The chiral Lewis acid species desired for the transformations was generated in situ. The phosphoramide **35** catalyzed the cross aldolization of aromatic aldehydes as well as aliphatic aldehydes with a silyl ketene acetal (Scheme 26)[93] with good yield and high enantioselectivity and diastereoselectivity.



Scheme 26

It was found that benzaldehyde reacts with *E* and *Z* configured silyl ketene acetals to furnish identical aldol products[93] with high enantioselectivity. Neither diastereoselectivity nor enantioselectivity were affected by double bond geometry of the silyl ketene acetal. This is an evidence for an acyclic transition state (Scheme 27).



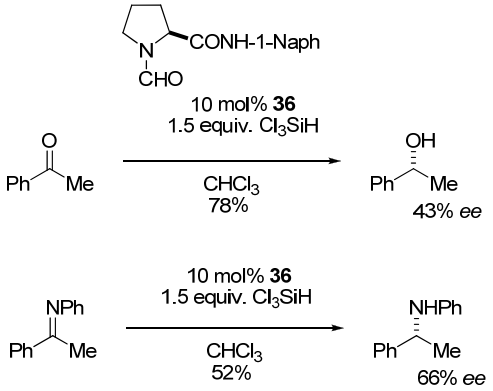
Scheme 27

Catalytic amount of **35** (1 mol%) also promoted the reaction of aromatic aldehydes with silyl ethers,[94] vinylogous silicon enolates[95] and even with isocyanates in the presence of stoichiometric amount of $SiCl_4$.[98] The products were isolated in high yield and enantioselectivity.

Next to phosphoramides, Denmark reported an axially chiral *N*-oxide to catalyze

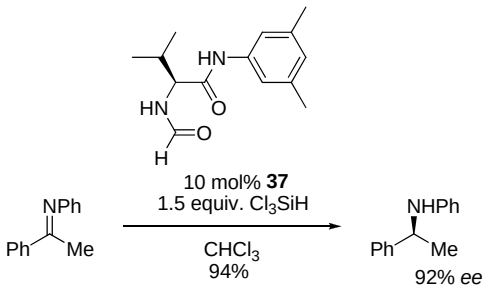
the asymmetric aldol reaction of trichlorosilyl enol ethers with ketones.[99] Hashimoto reported an aldol reaction with 3 mol% of another axially chiral *N*-oxide[100] which gave good yields and enantioselectivities.

Next, a few examples of asymmetric reductions with trichlorosilane are presented. An asymmetric reduction of ketones and imines was reported by Matsumura and coworkers by using trichlorosilane as reductant and *N*-formyl pyrrolidine derivative **36** as ligand (Scheme 28).[101, 102]



Scheme 28

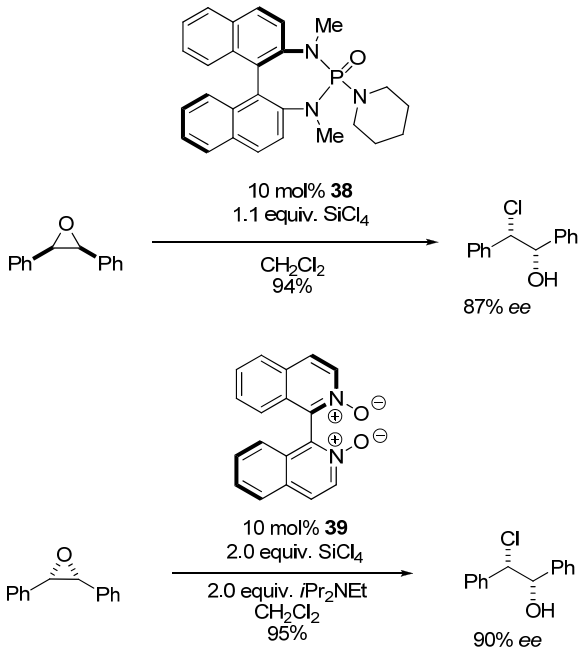
Later Malkov and Koĉovsky reported the asymmetric reduction of imines with *N*-methyl L-valine derivative **37** with high yield and enantioselectivity (Scheme 29).[103]



Scheme 29

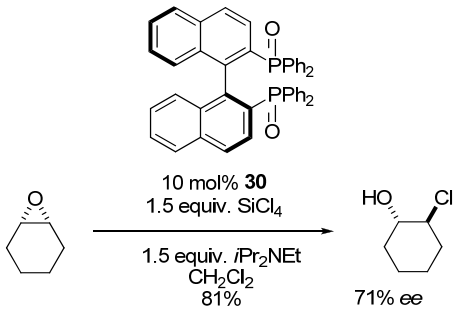
Next to the above presented use of $SiCl_4$ for the in situ preparation of a Lewis acid catalyst with a Lewis base for the aldol reaction, it is possible to apply this compound as a reagent in the ring opening of epoxides leading to chlorinated alcohols. Denmark[104] reported that the chiral phosphoramide **38** catalyzed the asymmetric ring opening reaction of meso-epoxides in the presence of

tetrachlorosilane. Similar examples were provided by Hashimoto in 2002,[105] applying the *N*-oxide **39** as catalyst (Scheme 30).



Scheme 30

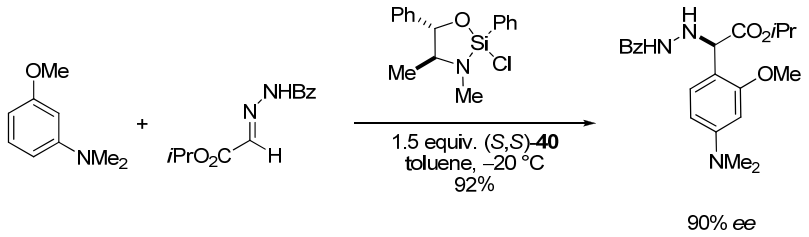
Later in 2005, Hashimoto[106] reported the asymmetric ring opening reaction of cyclohexane oxide with catalyst **30** and afforded the corresponding chlorohydrin in high yield and enantioselectivity (Scheme 31).



Scheme 31

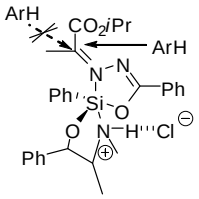
Extending the application of his *strained silacycle* reagents, Leighton et al. described a method for the enantioselective Friedel-Crafts alkylation with benzoylhydrazones, catalyzed by an extraordinarily simple chiral silane Lewis acid. The salient features of the chiral silane are: it can be prepared in bulk in a single step from (*S*,*S* or *R*,*R*) pseudoephedrine and $PhSiCl_3$, and after employing it in a reaction, pseudoephedrine can be recovered in nearly quantitative yield

during the workup. The best example is shown in Scheme 32 in which by employing chiral silane **40**, 92% yield and 90% *ee* of the product were achieved in 48 h.[107]



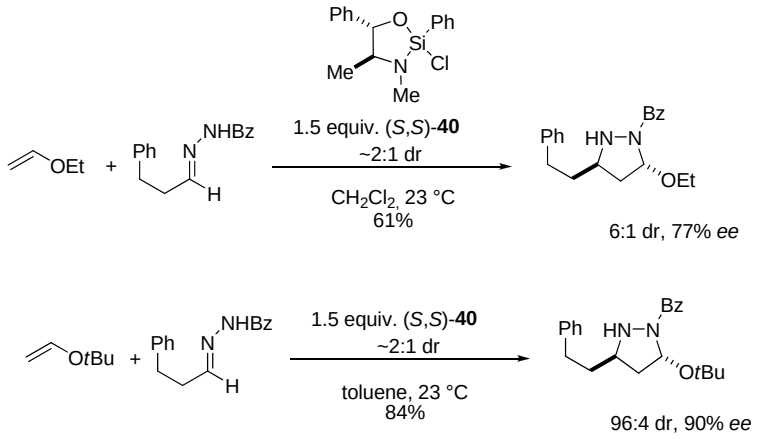
Scheme 32

The catalyst, although applied in 1.5 equiv., worked also well with heteroarenes in the alkylation reactions. A simple and most plausible mode for the enantioselectivity of the Friedel-Crafts reaction has been shown as following in Scheme 33. It is evident from the model that the arene would approach from the front (*Si*) face, as the back (*Re*) face is blocked by the phenyl group present on the silicon.



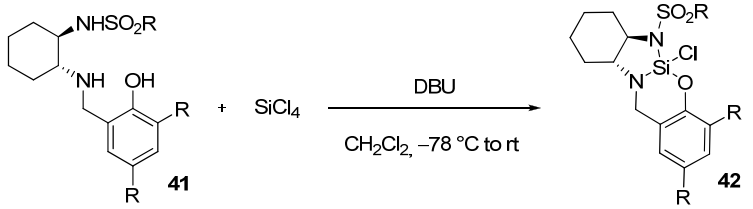
Scheme 33

Inspired by the previous results, Leighton et al. reported the enantioselective [3+2] acylhydrazone-enol ether cycloaddition reaction by employing the same pseudoephedrine based chiral silane. The pyrazolidine product was obtained in 61% yield with 6:1 dr and 77 % *ee* in 24 h. The use of *tert*-butyl vinyl ether led to an improvement in both diastereoselectivity and enantioselectivity as shown in Scheme 34.[108]



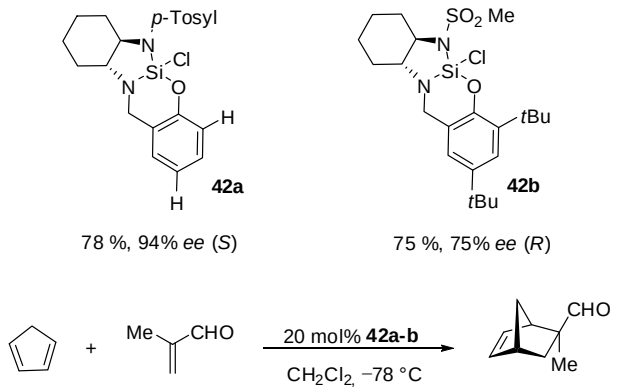
Scheme 34

In 2006 Leighton et al. reported that a chiral ligand carrying three functional groups for attachment to tetrachlorosilane, proved to be a good ligand for the efficient silane catalyst **42** in the cycloaddition reaction of enals with cyclopentadiene. The catalyst was generated in situ by treatment of **41** with $SiCl_4$ and DBU in 4 h (Scheme 35).[109] It was possible to assign the relative configuration of compound **42** at the silicon center by the observation of NOE interactions (Scheme 37).



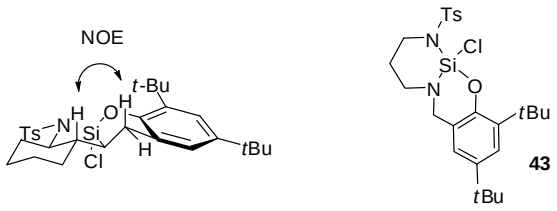
Scheme 35

Simple changes to a sulphonamide group and substituents on the phenols produced a dramatic effect on the enantioselectivity in the reaction (Scheme 36).



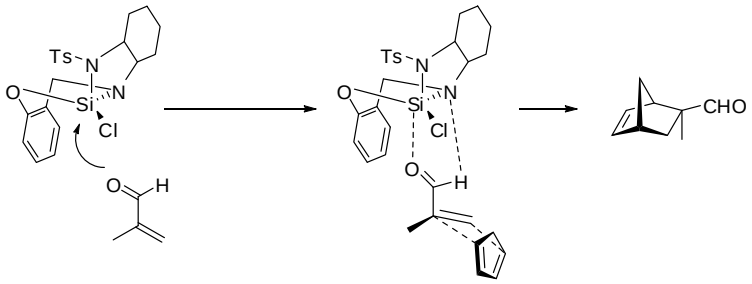
Scheme 36

It was proven that a 5-membered strained ring is an essential component for the Lewis acidity. Thus silane **43**, being 6-membered, is strain free and showed no catalytic activity under identical reaction conditions (Scheme 37).



Scheme 37

The proposed mechanism is depicted in Scheme 38. The aldehyde is activated due to coordination on the silicon atom. A hydrogen bond between the aldehyde function and the benzyl substituted tertiary nitrogen atom stabilizes the transition state, and the benzyl group ensures that the cyclopentadiene attacks the dienophile only from one side.

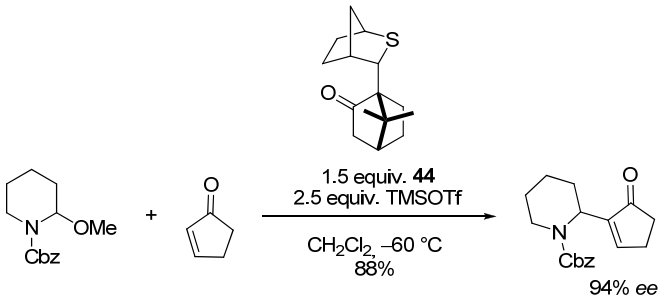


Scheme 38

Finally, a few examples of the Morita-Baylis-Hillman reaction are provided, where a silyl species functions as a Lewis acid co-catalyst. These examples could have been presented in the previous section about silyl cation based catalysts. Since the enantiomeric induction originated in the present examples from a Lewis base, we have listed these examples in this section.

The promoters of the so-called chalcogenide Morita-Baylis-Hillman reaction are Kataoka and co-workers who employed sulfide and $TiCl_4$ for dual Lewis acid-base activation. Later, in 1996 the ability of the combination of sulfide/TBDMSOTf to promote the reaction was reported.[110] Asymmetric version of the Baylis-Hillman reaction has been achieved by using chiral sulfide

in place of SMe_2. The best *ee* was 94% in combination with a high yield of 88% in 5 h (Scheme 39).[111]

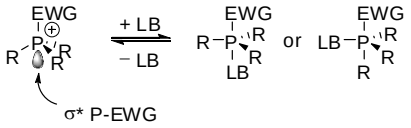


Scheme 39

In summary, it is possible to state, that the field of the Lewis base catalyzed reactions involving silane reagents, is very well established and high enantioselectivities can be obtained for several examples. As pointed out above the research field has been only briefly discussed in this review, since it is considered to be a Lewis base catalyzed domain. Since the reactive intermediate is a Lewis acid, it was decided to discuss it in the context of this article. Considering the examples where the silane reagent was replaced by $SiCl_4$ to generate in situ an active Lewis acid catalyst, one could argue that it is possible to place the reactions also under the category of Lewis acid catalyzed reactions. The presented example of the catalyzed Diels-Alder reaction with strained 5-membered silanes belongs undoubtedly to the field of Lewis acid organocatalysts.

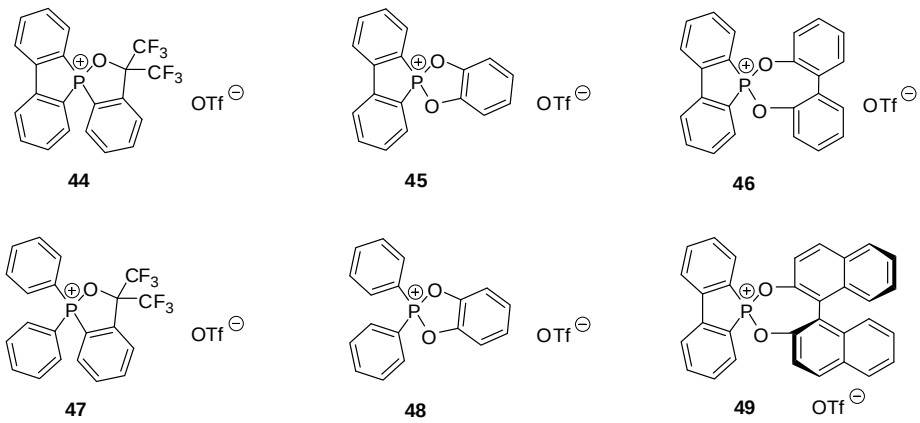
4 Phosphonium Cation Based Catalysts

In 2006 Terada and Kouchi reported the investigation of phosphonium salts in catalysis.[112] A pentacoordinated phosphorus atom is a hypervalent[113] atom, which has a formal valence shell of more than eight electrons. As shown in Scheme 40, it is possible for the lower lying σ* orbital of a P^+-EWG (Electron Withdrawing Group) bond to take up a free electron pair of a Lewis base, in order to form a new bond. If the new formed bond is *trans* to the EWG, the formed complex is more stable.



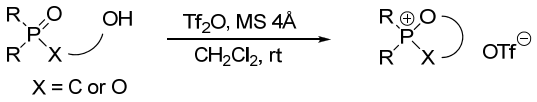
Scheme 40

The authors prepared a series of different phosphonium salts of which a few examples are given below. All incorporated electron withdrawing groups as shown in Scheme 41.



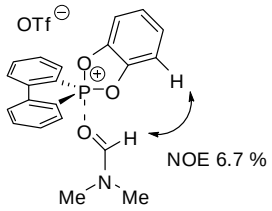
Scheme 41

The salts were prepared from hydroxy phosphine oxides or phosphinates as depicted in Scheme 42 after 1 h. The reactions were carried out with trifluoromethanesulfonic anhydride in the presence of 4Å molecular sieves, and it was shown by ^{31}P-NMR due to downfield shifts that the phosphonium salts were formed. However, the salts could not be isolated and were prepared in situ for NMR studies and for the application in catalysis.



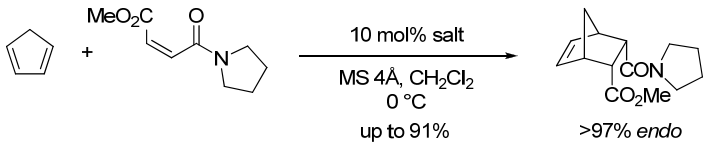
Scheme 42

In NMR investigations of the salts with DMF, it was possible to observe a shift change in the case of salts **45** and **48**. The other salts revealed no change. It appeared that the 5-membered ring of the catechol substituent is crucial for a high reactivity. It is known that cyclic 5-membered phosphorous compounds possess an enhanced reactivity.[114, 115] Salt **45**, incorporating two 5-membered rings, showed a stronger interaction with DMF than salt **48**. As shown in Scheme 43, an NOE was found between the C3-proton of the catechol moiety and the formyl proton of DMF.



Scheme 43

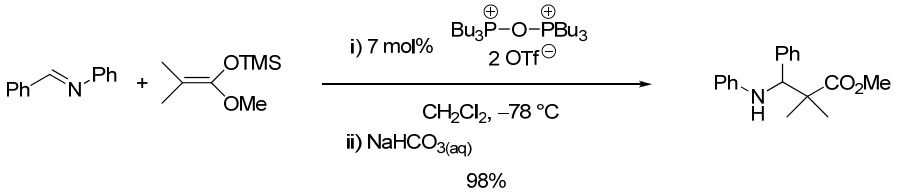
The authors investigated the salts in the Diels-Alder reaction. In analogy to the NMR experiments similar reactivities were found. As presented in Scheme 44, the salts gave up to 91% yield in high *endo*-selectivity with cyclopentadiene and an unsaturated amide in 4 h. The highest yield was obtained with salt **45**, while for example salt **47** gave only 7% and salt **49** gave only traces.



Scheme 44

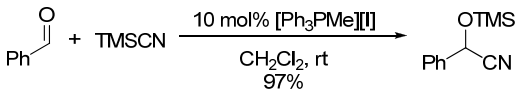
Already in 1989, Mukaiyama explored the behaviour of phosphonium salts as Lewis acid catalysts. It was possible to show that the aldol-type reaction of aldehydes or acetals with several nucleophiles and the Michael reaction of α,β-unsaturated ketones or acetals with silyl nucleophiles gave the products in good yields with a phosphonium salt catalyst.[116] In addition, the same group applied

bisphosphonium salts as shown in Scheme 45 in the synthesis of *β*-aminoesters.[117] High yields up to 98% were obtained in the reaction of *N*-benzylideneaniline and the ketene silyl acetal of methyl isobutyrate. Various analogues of the reaction partners gave similar results. The bisphosphonium salt was found to be superior to Lewis acids like $TiCl_4$ and $SnCl_4$, which are deactivated by the resulting amines.



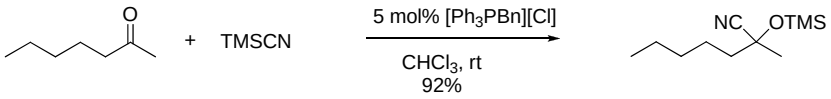
Scheme 45

Furthermore, phosphonium salts have been applied as catalysts in the TMSCN addition to aldehydes[118] and ketones.[119] Methyltriphenylphosphonium iodide[118] was found to be a reasonably active catalyst for the addition of TMSCN to aldehydes at rt by the group of Plumet. In general, the yields varied between 70% and 97% in 24 h, depending on the aldehyde, applied in the reaction (Scheme 46). However, the salt did not support the addition of TMSCN to ketones, with one exception, when the highly reactive cyclobutanone was applied in the reaction.[120]



Scheme 46

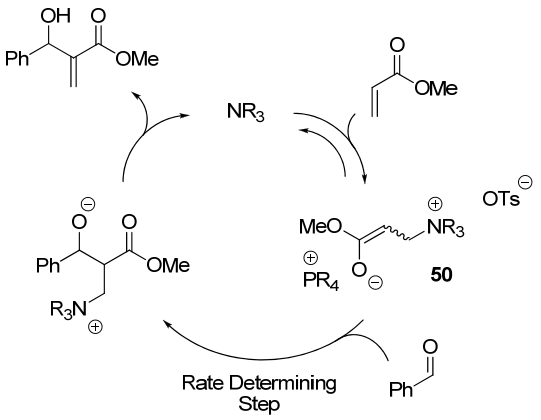
In order to extend the reaction to further ketones, it was found by the group of Tian,[119] that benzyltriphenylphosphonium chloride was a suitable phosphonium salt based catalyst which gave the desired product in 92% yield in the reaction of 2-heptanone with TMSCN in 24 h (Scheme 47). The authors could show that it was essential to apply the chloride salt in the reaction. In case a bromide analogue was used, only a yield of 2.6% was found.



Scheme 47

In the phosphonium iodide and chloride salt catalyzed TMSCN addition on aldehydes and ketones, a double activation should exist. Not only the activation of the ketones or aldehydes with the phosphonium cation is necessary, but also the activation of the TMSCN by the soft Lewis base [I] or the harder Lewis base [Cl], which can form a pentavalent silicon intermediate.[121]

Phosphonium salts have also been used as co-catalysts in the DABCO catalyzed Baylis-Hillman reaction of methyl acrylate with benzaldehyde.[122] Good results were obtained with triethyl-*n*-butylphosphonium tosylate with up to quantitative yields in some cases. The authors proposed that the phosphonium salt is rather stabilizing the intermediate **50**, shown in Scheme 48, and increasing therefore its concentration rather than activating the benzaldehyde.



Scheme 48

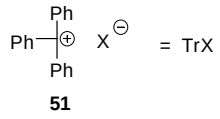
Finally, achiral phosphonium salts have been applied as Lewis acid catalysts in some other reactions. The examples will be listed here but not discussed in more detail. Phosphonium salts have been used as catalysts for the *N*,*N*-dimethylation of primary aromatic amines with methyl alkyl carbonates giving the products in good yields.[123] In addition acetonyltriphenylphosphonium bromide has been found to be a catalyst for the cyclotrimerization of aldehydes[124] and for the protection/deprotection of alcohols with alkyl vinyl ethers.[125, 126] Since the

pK_a of the salt is 6.6,[127-130] the authors proposed that next to the activation of the phosphonium center, a Brønsted acid catalyzed pathway is possible.

In summary, there are now several examples of phosphonium salt based Lewis acids as catalysts known, which have shown a good catalytic activity. However, an asymmetric catalyzed reaction with an enantiopure phosphonium salt has not been reported yet.

5 Carbocation Based Catalysts

During the past decades, the scope of Lewis acid catalysts was expanded with several organic salts. The adjustment of optimal counter anion is of significant importance, while it predetermines the nature and intensity of catalytic Lewis acid activation of the reactive species. Discovered over 100 years ago and diversely spectroscopically and computationally investigated,[131-133] carbocations still remain seldom represented in organocatalysis, contrary to analogous of silyl salts for example. The first reported application of a carbenium salt introduced the trityl perchlorate **51** (Scheme 49) as a catalyst in the Mukaiyama aldol-type reactions and Michael transformations (Scheme 50).[134-142]

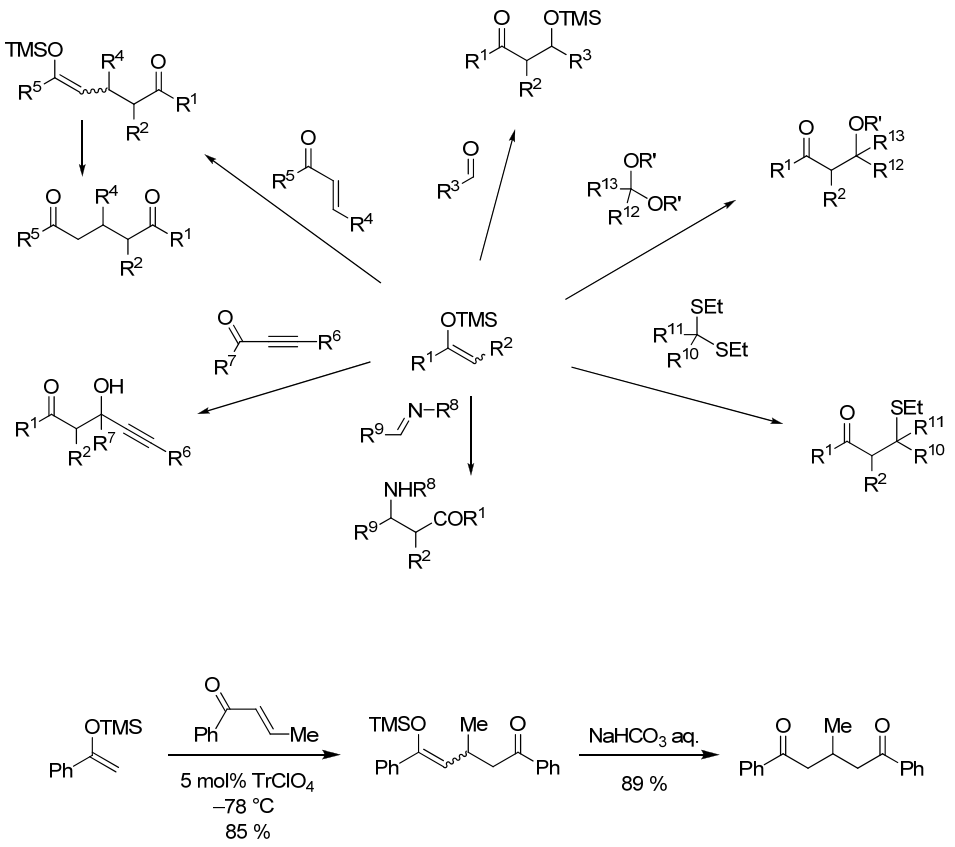


51

X = ClO_4, TfO, $SbCl_4$, BF_4

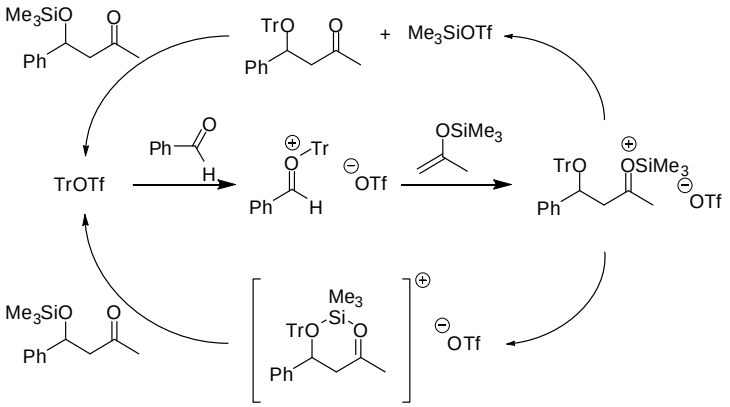
Scheme 49

The reactions proceeded efficiently under mild conditions in short time. The silyl enol ethers reacted with the activated acetals or aldehydes at –78 °C to give predominant erythro- or threo-products[136, 137] respectively. In the same manner, the aldol reaction of thioacetals, catalyzed by an equimolar amount of catalyst, resulted in γ-ketosulfides[139] with high diastereoselectivity. In the course of this investigation, the interaction of silyl enol ethers with *α,β*-unsaturated ketones, promoted by the trityl perchlorate, was shown to proceed regioselectively through 1,2-[141] or 1,4-addition.[138] The application of the trityl salt as a Lewis acid catalyst was spread to the synthesis of *β*-aminoesters[142] from the ketene silyl acetals and imines resulting in high stereoselective outcome.



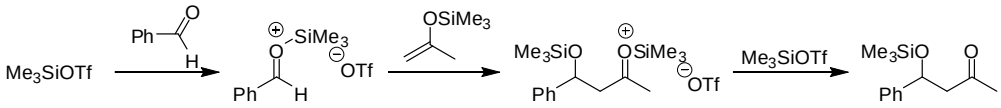
Scheme 50

The undefined mechanism of the aldol-type Mukaiyama and Sakurai allylation reactions arose the discussion and interest in mechanistic studies.[143-145] The proposed mechanism was proved to proceed through the catalytic activation of the aldehyde and its interaction with the silyl ketene acetal or allylsilane producing the intermediate. From that point the investigation is complicated with two possible pathways that lead either to the release of TMS triflate salt and its electrophilic attack on the trityl group in the intermediate or to the intramolecular transfer of the TMS group to the aldolate position resulting in the evolution of the trityl catalyst and the formation of the product (Scheme 51). On this divergence, series of experimental and spectroscopic studies were conducted.



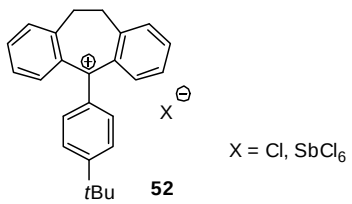
Scheme 51

The valuable and versatile study was conducted by the group of Bosnich.[143] The defined nature and amounts of by-products in the reaction mixture allowed to judge about the possible mechanism of the catalysis. It was proved that the aldolization and allylation reactions proceed with the evolution of TMS salt that is itself a strong Lewis acid and can catalyze the reaction in high rate (Scheme 52). The possible sources of the TMS salt production in the reaction medium were investigated. The utilization of a hindered base suppressed the influence of the silyl salt, and the rate of the reaction was dramatically diminished. This consequence was considered to confirm that the TMS salt can catalyze the reaction even in the undetectable quantities of 10^{-7} mol.



Scheme 52

The further investigation of functionalized trityl cations with different counter anions and TMS or TBS enolates, conducted by Chen,[145] introduced the dibenzosuberone-derived salt **52**[146] as a catalyst (Scheme 53).

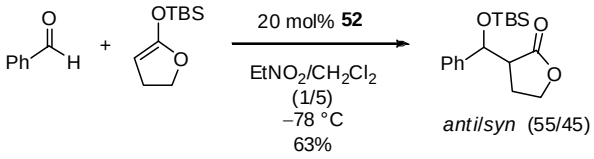


X = Cl, $SbCl_6$

52

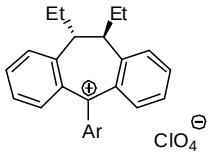
Scheme 53

The TBS ketene acetal was proposed to be the preferable silyl component, while the rate of the TBS transfer to the aldolate group of the product decreased and did not overtake the slow-acting carbenium catalysis (Scheme 54).



Scheme 54

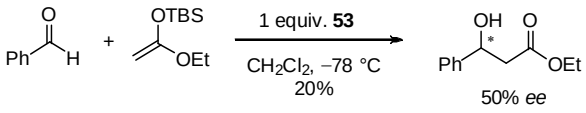
The next investigation conducted by the group of Chen,[147] involved the chiral trityl salt **53** and thus brought clearness to a certain extent in the understanding of the mechanism of the catalysis (Scheme 55). Since enantiomeric excess was achieved, the carbenium-mediated catalysis should not be disregarded. The correlation of the results manifested the concurrence of the catalytic species and dependence of their participation in the catalysis on the silyl substituents and counter ions in the trityl salts.



53

Scheme 55

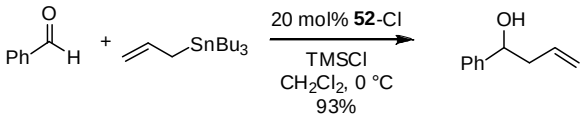
Over a reaction period from 3 to 6 h (Scheme 56) the enantioselectivity of the aldolization catalyzed by **53** decreased from 24 % to 11 % along with the increase of yield from 52 % to 99 %. The decrease of the enantioselectivity with prolongation of reaction time indicates the prevailing of the silyl-mediated catalysis, due to the slow metathesis between tritylated aldolate and silyl salt. The best enantioselectivity of 50 % together with just 22 % yield was achieved when 1 equiv. of catalyst **53** was used. This experiment points out the slow consumption of trityl ions as well as the low rate of the silyl substitution of the trityl aldolate.



Scheme 56

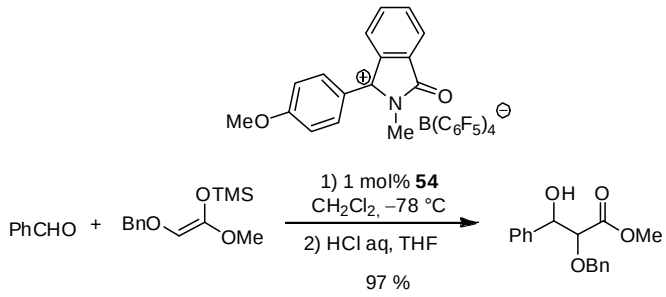
The estimation of the conditions, suppressing the silyl-mediated catalysis and preferable for the carbenium-promoting catalysis, is of significant importance to introduce the chiral information in the product. Since it was observed that a carbenium salt promoted the reaction and thus provided the enantioselectivity in the outcome, the rigid conformation and the enhanced reactivity of the carbocation may be the key requirement for the productive enantioselective carbenium catalysis in the aldol-type additions.

The catalytic activity of the trityl moiety was unobjectionably adjusted in the addition reaction of the allylstannanes to aldehydes.[148] In this allylation process the trityl chloride **52**, due to its disposition to partially ionic character of the halogen bonding, was employed as a catalyst in the complementary tandem with weak Lewis acid TMSCl (Scheme 57). The excess of the silyl component was necessary, in order to release the trityl catalyst from the intermediate to complete the catalytic cycle. The achieved yield was 93%, when trityl chloride **52** was used.



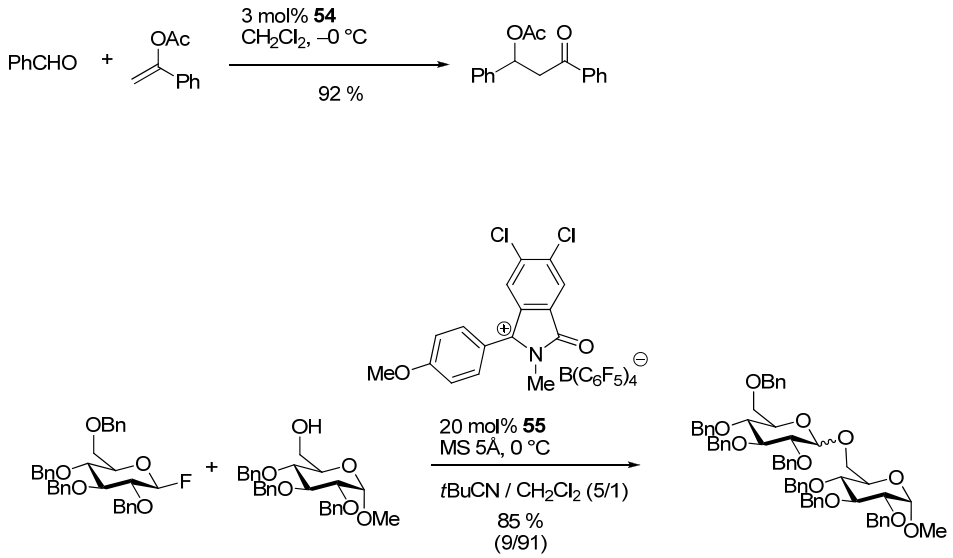
Scheme 57

In order to enhance the catalytic activity of a carbocationic center, the novel Lewis acid **54** was designed by Mukaiyama.[149-152] The 1-oxoisoindolium-based carbenium salt **54**,[149] possessing a weak coordinating borate counter anion, proved to be a very active catalyst in the aldolization (Scheme 58).[150] The Mukaiyama aldol reaction was catalyzed by 1 mol% of salt **54** and proceeded in up to 97% yield in 30 min.



Scheme 58

The catalytic activity of the oxoisoindolium salt **54** and **55** was compared to that of trityl tetrakis[pentafluorophenyl]borate salts in the addition reaction of enol acetate to benzaldehyde and glycosylation reaction (Scheme 59).[151, 152]

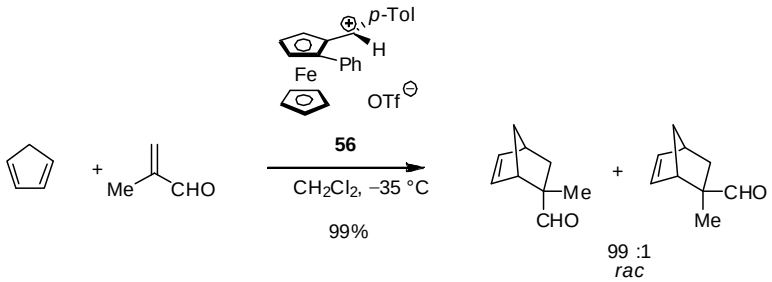


Scheme 59

The utilization of compound **54** in the aldolization showed higher yield of the product (92%) after 30 min, compared to that (73%) of a trityl catalyzed reaction. The similar results were obtained in the glycosylation reaction: 85% (*α/β* ratio 9:91) and 72% (*α/β* ratio 10:90) respectively. The application of the highly hindered tetrakis[pentafluorophenyl]borate anion is remarkably advantageous for the stabilization of the positive charge in the carbocation **54** and at the same time promotion of its accessibility to the interaction with a carbonyl species.

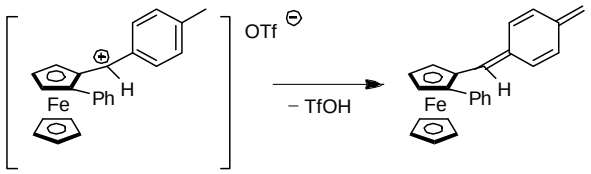
The development of the stable *α*-ferrocenyl carbocations **56** prompted the further investigation of the carbenium salts in the Lewis acid catalyzed reactions (Scheme 60). The group of Kagan[153-155] designed the *o*-substituted ferrocenyl scaffold

that allowed to avoid the placement of two aryl groups on the carbocation and provided the stabilization and asymmetry, preventing the isomerization by the facile rotation about the carbenium center. Being exploited in the Diels-Alder reaction of cyclopentadiene with methacrolein, the catalyst **56** displayed a perfect *exo*/*endo* diastereoselectivity of up to 99:1 in the presence of 4Å MS resulting in nearly quantitative yield (Scheme 60).



Scheme 60

Contrarily to these results, the group of Sammakia[156] reported that the reaction can be actually catalyzed by the protic acid TfOH, released either by the decomposition of the carbenium salt or by the nucleophilic attack of the diene on the cation center with evolution of the proton.



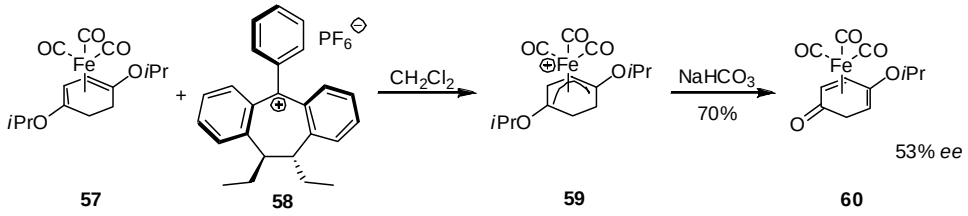
Scheme 61

Supplementary studies of the mechanism were conducted. The dependence of the reaction rate on the nature of environment at the cationic carbon has shown that the concurrent formation of the protic acid proceeds, if the substituents can undergo the isomerization (Scheme 61), and thus the carbenium catalysis is utterly negligible. It was shown that the reaction was still catalyzed, even when a base was added in order to rule out a TfOH catalyzed reaction. Obviously, the protonated base was then a catalyst.

While the ambiguity of the catalysis of the Diels-Alder reaction needs to be carefully elucidated, the application of the ferrocenyl carbocations in the

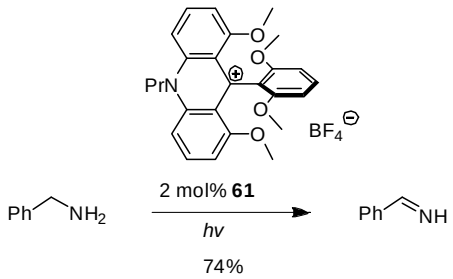
Mukaiyama aldolization turned out evidently to be unrealisable due to their interaction with the TMS enol ether that produces TMSOTf, which proved readily to catalyze the aldolization.[154]

Due to the extensively represented oxidative behaviour of the carbenium ions as hydride abstractor or one-electron oxidant,[157] attempts were made to employ the carbocations as reagents. Recently the enantioselective outcome in a hydride transfer reaction was reported.[158, 159] The abstraction of the *exo* hydrogen atoms from the tricarbonyliron complex **57** resulted in a yield up to 70% and enantioselectivity of 53% (Scheme 62).[158]



Scheme 62

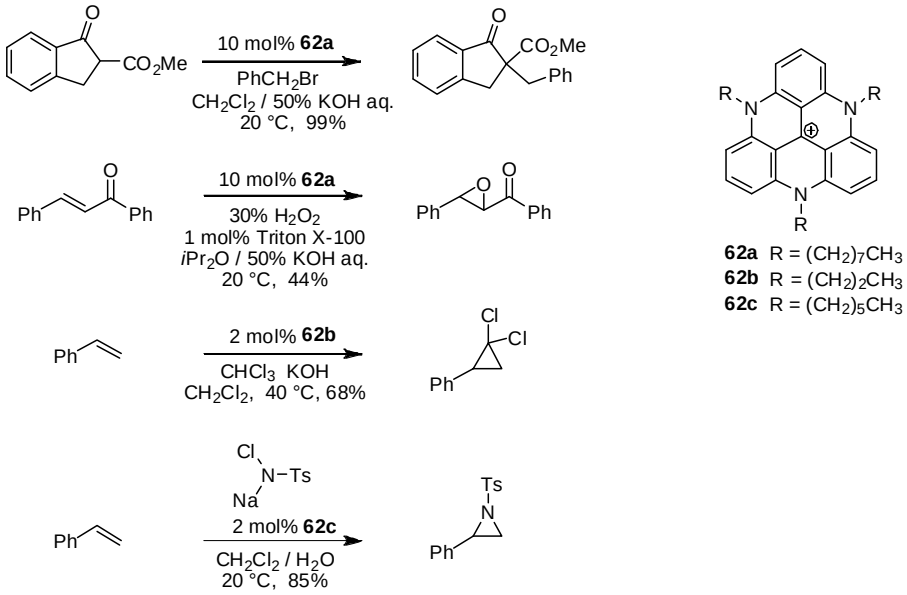
Also the oxidative behaviour of the acridinium carbocations **61** was explored by the group of Lacour in the photoinduced electron transfer reaction.[160] In the amount of 2 mol%, the achiral hindered acridinium salt **61** catalyzed the aerobic photooxidation of the primary benzylic amine to benzylimine in the yield of 74% (Scheme 63).



Scheme 63

Finally, one example of trityl salt analogues in the phase-transfer catalysis is presented. The highly stable triazatriangulenium cations **62**[161, 162] were just recently introduced to the phase-transfer chemistry.[163] Persistent to strongly basic and nucleophilic conditions, these salts revealed efficient catalytic activity

in addition reactions (Scheme 64). Modification of the alkyl side chains on nitrogen allowed matching the fair hydro/lipophilicity with the optimised conditions in the alkylation, epoxidation, aziridination and cyclopropanation reactions. The results are comparable to those of tetrabutylammonium salts and in some cases showed even a better outcome.



Scheme 64

So far, there has been only one example of a successful asymmetric catalyzed reaction with an enantiopure carbocation based salt. In this section it was possible to learn, that a good understanding of a catalyzed reaction is necessary and that possible achiral side reactions have a critical negative influence. Nevertheless, carbocations can be highly active catalysts. However, this makes their application sometimes difficult. One exception was the last presented example resembling a moisture, base and nucleophilic stable trityl cation. In the next chapter ionic liquids will be discussed, some of which can be also classified as carbocation based salts. However, they are far more stable but on the other hand possess a lower catalytic activity.

6 Ionic Liquids

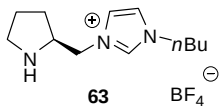
Ionic liquids, having per definition a melting point below 100 °C, and especially room temperature ionic liquids (RTIL) have attracted much interest in recent years as novel solvents for reactions and electrochemical processes.[164] Some of these liquids are considered to be "green solvents".[165] The scope of ionic liquids based on various combinations of cations and anions has dramatically increased, and continuously new salts[166-168] and solvent mixtures[169] are discovered. The most commonly used liquids are based on imidazolium cations like 1-butyl-3-methylimidazolium [bmim] with an appropriate counter anion like hexafluorophosphate [PF_6]. Salts with the latter anion are moisture stable and are sometimes called third generation ionic liquids.

The so called second generation ionic liquids were prepared from organic cations and $AlCl_x$ anions.[170] Since $AlCl_3$ was present in these liquids, they were used as catalysts in Lewis acid catalyzed reactions. Also many of the third generation ionic liquids have been used as solvents for catalytic reactions.[171-174] However, it is also known that third generation ionic liquids are capable of catalyzing reactions, either in substoichiometric amounts or as reaction medium. This will be discussed in this section.

There have been recently several reviews about the preparation and application of chiral enantiopure ionic liquids.[172, 175-177] Unfortunately, often the evaluation of the growing number of enantiopure ionic liquids concentrated more on their behavior as chiral discrimination agents. Hence, the number of examples of reactions catalyzed by enantiopure ionic liquids is rather small, and therefore this section will also give an overview over catalyzed reactions with achiral ionic liquids, rather than giving examples of enantiopure ionic liquids, which have not been evaluated as reaction medium yet.

Examples, like the application of enantiopure ionic liquids in the copper catalyzed enantioselective 1,4-addition of diethyl zinc to enones giving up to 76% *ee*, will not be presented,[178] since here the chiral ionic liquid, CIL, acts as a ligand for a metal catalyzed reaction.

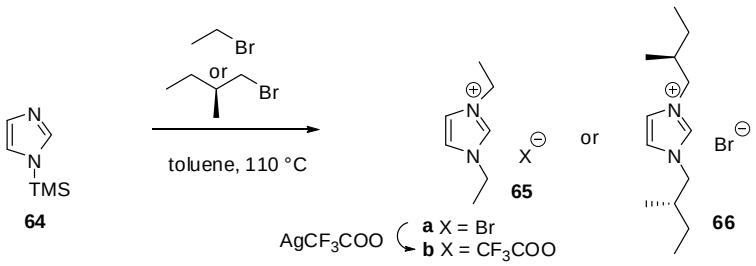
Furthermore, to clarify the difference between task specific ionic liquids (or also called functionalized ionic liquids) and chiral ionic liquids, one very successful example of a task specific ionic liquid **63** is presented in Scheme 65. This catalyst with a loading of 15 mol% under neat conditions gave up to 100% yield and 99% *ee* in the Michael addition of cyclohexanones to nitroolefins.[179] This catalyst belongs to the field of the proline catalyzed reactions.



63

Scheme 65

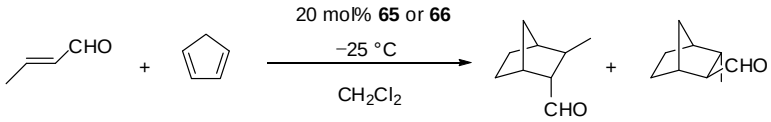
In 1997 Howarth[180] reported the preparation of ionic liquids **65** and **66**. They presented, that imidazolium cations can be used as Lewis acid centers in catalytic amount rather than as solvent (Scheme 66). The bromide salts **65a** and **66** were prepared by a literature procedure[181] from TMS protected imidazole **64** and ethyl bromide or (*S*)-1-bromo-2-methylbutane in refluxing toluene in 46% and 21% yield, respectively. Salt **65a** was converted into salt **65b** with $AgCF_3COO$ in 89% yield.



64 **65** **66**

Scheme 66

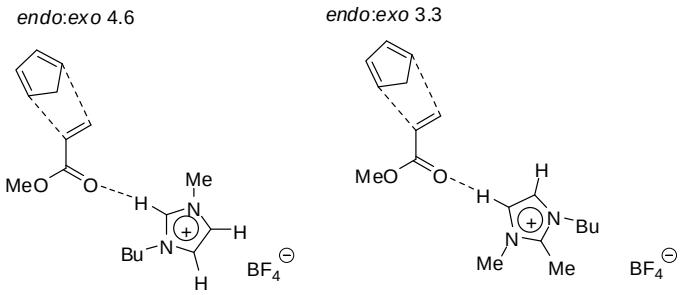
The salts were investigated in the Diels-Alder reaction of crotonaldehyde with cyclopentadiene (Scheme 67). The obtained yields were between 35 and 40% with an *endo*:*exo* ratio of 90:10. The control reaction without the salt at –25 °C gave no product. The observed *ee* with the enantiopure salt **66** was less than 5%. Nevertheless, this was the first example which showed, that imidazolium based ionic liquids can be used in substoichiometric amounts as Lewis acid catalysts.



Scheme 67

Also the use of moisture stable ionic liquids as solvents in the Diels-Alder reaction has been carried out, and in all examples an enhanced reaction rate was observed.[182, 183] The application of pyridinium based ionic liquids allowed the utilization of isoprene as diene.[184] The chiral ionic liquid [bmim][L-lactate] was used as a solvent and accelerated the reaction of cyclopentadiene and ethyl acrylate, however, no enantiomeric excess was observed.[183] In addition several amino acid based ionic liquids have been recently tested in the Diels-Alder reaction. Similar *exo*:*endo* ratios were found but the product was obtained as racemate. The ionic liquids were prepared by the addition of equimolar amounts of HNO_3 to the amino acids.[185] Furthermore, an enantiopure imidazolium salt incorporating a camphor motive was tested in the Diels-Alder reaction. No enantiomeric excess was found.[186]

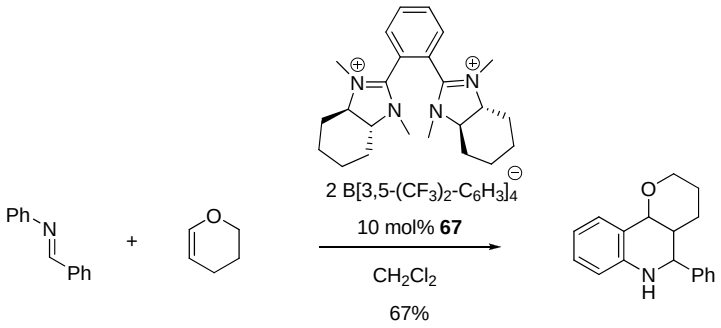
In order to investigate the origin of the catalytic activity of imidazolium based ionic liquids, the group of Welton[187] performed further studies, and it was proposed that hydrogen bond activation plays an important part in the activation of a dienophile in the Diels-Alder reaction. This was proposed due to observed hydrogen bonds between the imidazolium cation and the corresponding counter anion in the salt. The reaction of methyl acrylate in the ionic liquid [bmim][BF_4] with cyclopentadiene gave the product in 72 h at 25 °C in 85% yield. When the C2-methylated salt [bm_2im][BF_4] was applied as solvent, a similar yield of 84% was obtained, however, the *endo*:*exo* ratio changed from 4.6 to 3.3. This was attributed to weaker hydrogen bond formation with the C4 and C5 protons compared to the C2 proton in the first salt (Scheme 68).



Scheme 68

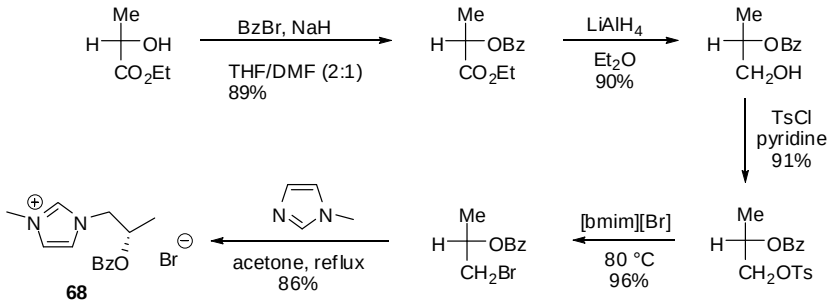
This would place imidazolium based ionic liquids more to the hydrogen bond activator organocatalysts. However, further studies by the group of Dyson showed that when salt analogues with [NTf_2] as the counter anion were used in the reaction, the salt with a methyl group at the C2 position gave a better *exo*:*endo* selectivity, indicating that hydrogen bond capability is not the only reason for the activity of the imidazolium ionic liquids, and other variables, like π-orbital interactions have to be taken into account.[188] Recent calculations for an imidazolium salt showed, that the hydrogen bond of a C2-H of the imidazolium cation with a corresponding counter anion is considerably different from that of conventional hydrogen bonds and not as strong as previously considered. The charge-charge interaction of the ion pair was proposed to be the dominant interaction.[189]

The ionic liquid [bmim][BF_4] is known to catalyze the aza-Diels-Alder reaction in the synthesis of pyrano- and furanoquinolines.[190] This reaction was also catalyzed by the enantiopure bis-imidazolinium salt **67** in 67% yield with an *endo*:*exo* ratio of 60:40 (Scheme 69).[191] The product was obtained as a racemate. In addition the aza-Diels-Alder reaction with imines and Danishefsky´s diene was catalyzed by the salt **67** giving racemic product. The salt and its analogues could be easily prepared via the oxidation of the corresponding aminals.[192] Investigation of the influence of the counter anion in achiral C2-substituted imidazolinium salts, which can be also described as 4,5-dihydroimidazolium or saturated imidazolium salts, in the aza-Diels-Alder reaction showed, that the catalytic activity increased, the more lipophilic the counter anion and therefore the more hydrophobic the salt was.[193]



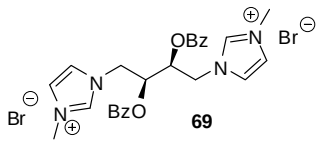
Scheme 69

The chiral ionic liquids **68** and **69** have been recently prepared and tested in the Michael addition (Scheme 72).[194] The chiral salt **68** was prepared as shown in Scheme 70 in an overall yield of 60% from L-(−)-ethyl lactate.



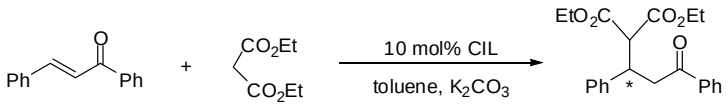
Scheme 70

Also the salt **69** was prepared in a similar way from L-(+)-diethyl tartrate in an overall yield of 44% (Scheme 71).



Scheme 71

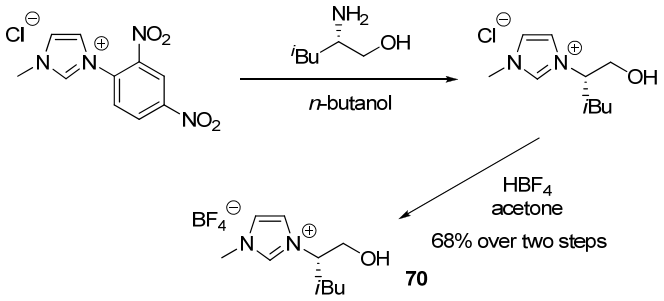
The salt **68** gave under solid phase transfer conditions a yield of 96% and 25% *ee* at rt. Since the melting point of the CIL was over 40 °C, toluene was used as a solvent. The influence of different anions in the salt was very low. Compared to the [Br] counter anion, [PF_6] resulted in 23% *ee* and [BF_4] gave an *ee* of 24%. When the polar solvents DMSO and DMF were investigated, a decrease of the *ee* to 17 and 16% *ee* was observed. Salt **69** gave a lower *ee* of 10%. The enantiomeric excess was determined by optical rotation.



CIL **68** = 96%, 25% *ee*
CIL **69** = 95%, 10% *ee*

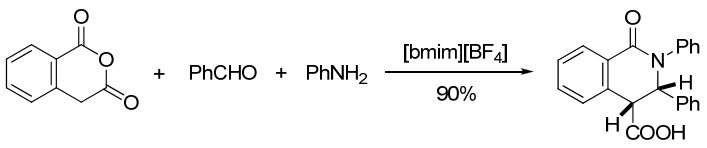
Scheme 72

Recently another enantiopure ionic liquid was tested in this reaction, and an *ee* up to 15% was obtained with the ionic liquid **70** which was prepared in an overall yield of 68% in two steps as shown in Scheme 73.[195]



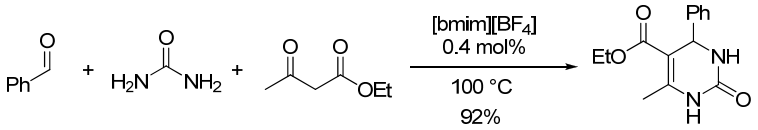
Scheme 73

The achiral ionic liquid [bmim][BF_4] was able to catalyze the three component reaction of benzaldehyde, aniline and homophthalic anhydride in 90% yield. Next to the major *cis*-isomer, 10% *trans*-isomer was isolated after 3 h (Scheme 74).[196] Control reactions in CH_2Cl_2 with 10 mol% [bmim][BF_4] and without catalyst showed that in the presence of the ionic liquid a high conversion in a short time was observed. Application of polar solvents like methanol or acetonitrile made it necessary to increase the reaction temperature to 70-80 °C, and the product was obtained in only 45-60% yield in a prolonged reaction time of 8-15 h. Further control reactions with [nBu$_4$N][Cl] or [bmim][Cl] showed that the anion played a comparable important role as the cation, since no product was formed. The author could demonstrate the generality of the reaction by the application of a broad variety of benzaldehyde and aniline derivatives.



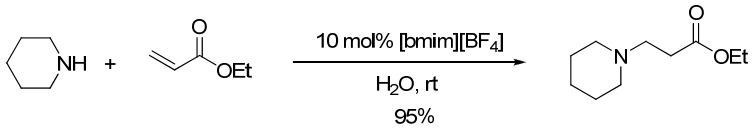
Scheme 74

The Biginelli reaction is also known to be catalyzed by the ionic liquids [bmim][BF_4] and [bmim][PF_6] under solvent-free conditions.[197] One example is shown in Scheme 75. While a control reaction without ionic liquid gave no product, the addition of just 0.4 mol% afforded a yield of 92% in 30 min. [Bmim][Cl] resulted only in a yield of 56%, while [$n$$Bu_4N$][Cl] gave no yield. This indicated that both the cation and the anion have an influence in catalyzing the reaction.



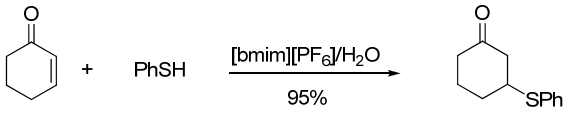
Scheme 75

The imidazolium based ionic liquid [bmim][BF_4] has been used as a catalyst in the aza-Michael reaction of various aliphatic amines to unsaturated compounds with different electron withdrawing groups in good yields as shown in Scheme 76. Water was used as the solvent in order to obtain up to 98% yield in 7 h. In the presented example, 95% yield in 7 h was achieved.[198] The ionic liquid could be recovered and reused five times without loss of activity.



Scheme 76

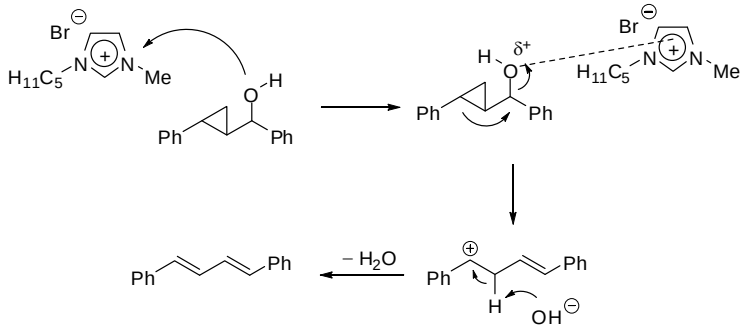
The addition of thiols to α,β-unsaturated ketones with [bmim][PF_6] in water was investigated. It was found that product could be obtained in up to 95% yield in 10 min (Scheme 77).[199]



Scheme 77

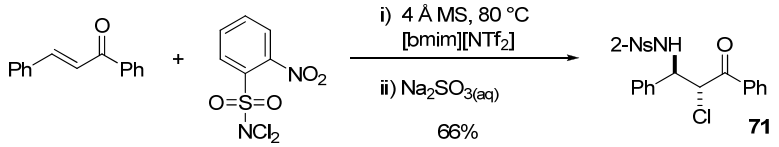
In addition, a Lewis acid behaviour was proposed in the cyclopropyl carbonyl rearrangement catalyzed by [pmim][Br] as depicted in Scheme 78.[200] The

products were obtained in good yields up to 95% when stirred at rt in the ionic liquid. By the application of sonication, the reaction time was decreased to 0.75 h.



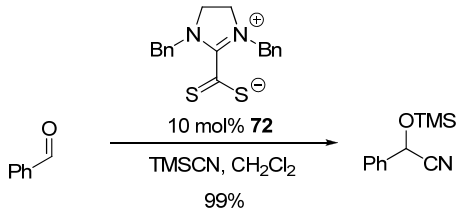
Scheme 78

The ionic liquid [bmim][NTf_2] catalyzed the aminohalogenation of electron-deficient alkenes in good yields. This is the first time that this reaction was performed in the absence of a metal catalyst. A representative example is presented in Scheme 79. The authors found that the major regiomer was **71**.[201]



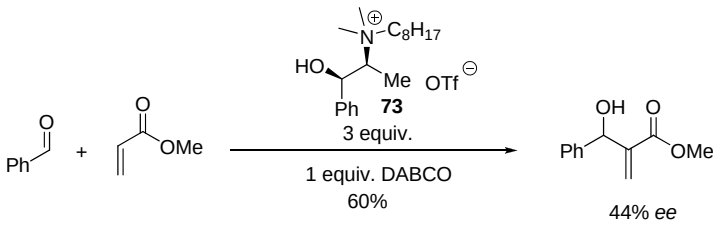
Scheme 79

The TMSCN addition on aldehydes has been reported to be catalyzed by the ionic liquid [omim][PF_6].[202] The influence of the counter anion in activating the TMSCN cannot be neglected, since the TMSCN addition on aldehydes can be also catalyzed by a Lewis base. The imidazolinium-dithiocarboxylate **72** has been recently shown to catalyze the reaction also in good yields up to 99% (Scheme 80).[203] One could assume, that the zwitterion incorporates a Lewis acid and Lewis base center. The reaction did not proceed in the absence of the catalyst.



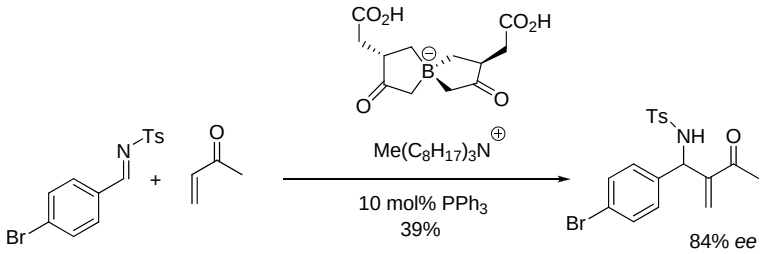
Scheme 80

Ionic liquids have been also explored in the Baylis-Hillman reaction.[204-206] The application of the enantiopure ionic liquid **73** in the Baylis-Hillman reaction by Vo-Thanh[207] resulted in an enantiomeric excess of up to 44% with 1 equiv. of the Lewis base catalyst DABCO (Scheme 81). It was shown that it was essential to have a hydroxy group incorporated in the ionic liquid in order to obtain significant *ee*.



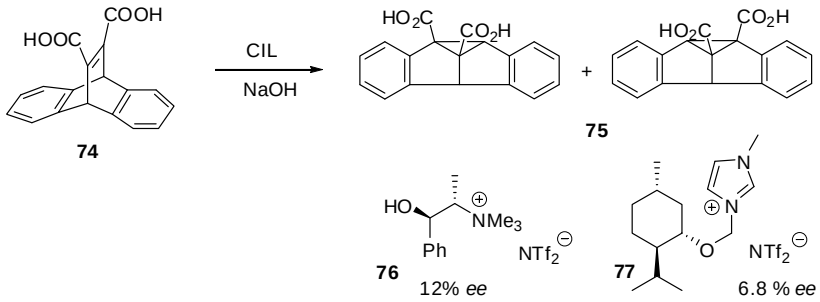
Scheme 81

Recently the group of Leitner was able to achieve high enantioselectivities in the aza-Baylis-Hillman reaction by the application of enantiopure ionic liquid with a chiral anion (Scheme 82).[208]



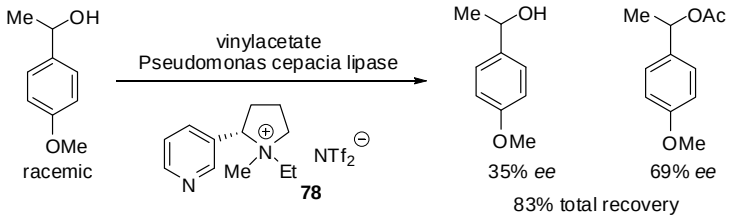
Scheme 82

Recently the group of D. W. Armstrong exploited the enantiopure ionic liquid **76** in the photoisomerization of dibenzobicyclo[2.2.2]octatrienes, and up to 12 % *ee* was reported (Scheme 83). The obtained *ee* was possible due to the addition of base in order to deprotonate the carboxylic acid function of **74** resulting in a strong anion – chiral cation interaction. In the absence of a base, lower values of *ee* were obtained, and in case that ester functions instead of carboxylic acid groups were present in the molecule, only racemic product was found. Ionic liquid **77** gave up to 6.8 % *ee*.



Scheme 83

The enantiopure nicotinium based ionic liquid **78** has been explored in the biocatalyzed kinetic resolution of 1-(4-methoxyphenyl)-ethanol with pseudomonas cepacia lipase (Scheme 84).[209] The obtained *ee* at rt without any other co-solvent however was lower compared to other systems.



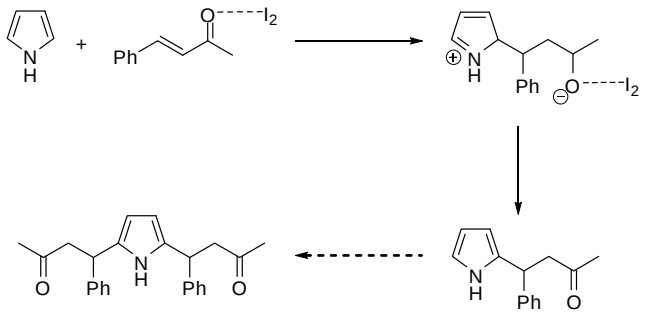
Scheme 84

Ionic liquids also showed a catalytic activity for the cyclocondensation of α-tosyloxyketones with 2-aminopyridine,[210] the nucleophilic substitution of α-tosylketones with potassium salts of aromatic acids,[211] the synthesis of aryl hydrazones,[212] the nucleophilic substitution reactions of highly functionalized allyl halides,[213] the alkylation of isobutene with 2-butene,[214] the Nazarov cyclization,[215] the Pictet-Spengler reaction,[216] the demethylation of *N*,*N*-dimethylanilines with phenyl chloroformate,[217] the alkylation of ammonium salts,[218] the aza-Michael reaction,[219] the aza-Markovnikov´s addition with *N*-heterocycles and vinyl esters,[220] the ring opening of epoxides with thiophenols,[221] the α-halogenation of β-dicarbonyl compounds and cyclic ketones with *N*-halosuccinimides,[222] and the ring opening of epoxides with TMSCl.[223] The listed examples were all carried out with achiral ionic liquids and will not be described in further detail, since the presented achiral examples so far have already displayed in general the catalytic activity of ionic liquids for different types of reactions.

Although the number of enantiopure ionic liquids as successful asymmetric catalytic reaction media is still very limited, the research field has attracted considerable attention. Due to the large number of possible applications in combination with the advantages of easy recoverability, the further development of the field is very important. However, it shall be mentioned here, that some reported examples of catalytic activities of ionic liquids have to be investigated in more detail. Especially ionic liquids incorporating $[BF_4]$ and $[PF_6]$ have to be very pure and normally should not be used with water for a prolonged time, since the anions could decompose and release HF, which could be itself the cause of the observed activity.[164]

7 Miscellaneous Catalysts

Iodine has been reported to possess a mild Lewis acidity and can activate carbonyl groups. It can for example catalyze the addition of pyrroles to α,β-unsaturated ketones (Scheme 85).[224] A mixture of pyrrol and 3 equiv. of ketone gave disubstituted products in up to 92% yield in 10 min with 10 mol% of iodine. In cases when only 1.1 equiv. of ketone was applied in the reaction, mono- and disubstituted products were isolated in few minutes in up to 95% yield in a ratio between 1:1 and up to 1:5. *N*-Alkylated pyrroles participated also in the reaction in good yields.



Scheme 85

In addition, iodine successfully catalyzed the electrophilic substitution reaction of indoles with aldehydes and ketones to bis(indonyl)methanes,[225] the deprotection of aromatic acetates,[226] esterifications,[227] transesterifications,[227] the chemoselective thioacetalization of carbon functions,[228] the addition of mercaptans to α,β-unsaturated carboxylic acids,[229] the imino-Diels-Alder reaction,[230] the synthesis of *N*-Boc protected amines,[231] the preparation of alkynyl sugars from D-glycals,[232] the preparation of methyl bisulfate,[233] and the synthesis of β-acetamido ketones from aromatic aldehydes, enolizable ketones or ketoesters and acetonitrile.[234]

Iodine is known to catalyze the condensation of aldehydes, benzyl carbamate and allyltrimethylsilane to homoallylic amines. However, in this case the involvement of an in situ prepared [Me_3Si] species was suggested to be the active catalyst.[235] An iodine catalyzed acetalization of carbonyl compounds was reported, where the active catalyst was believed to be hydroiodic acid.[236]

Very recently Ishirihara et al.[237] reported the application of a “chiral iodine atom” through the reaction of NSI and a chiral nucleophilic phosphoramidite for the halocyclization of homo(polyprenyl))arenes.

Next to iodine there is also another class of neutral Lewis acids known. Tetracyanoethylene, dicyanoketene acetals and derivatives can catalyse reaction due to their π-Lewis acid properties. They promoted the alcoholysis of epoxides,[238] tetrahydropyranylation of alcohols,[239] monothioacetalization of acetals,[240] and carbon-carbon bond formation of acetals[241, 242] and imines[243] with silylated carbon nucleophiles.

Recently, Denmark reported, based on the Lewis base activation of Lewis acids concept, a Lewis base catalyzed selenolactonization.[244]

While the research filed of selenium catalyzed reactions appears to be promising, the application of iodine as a catalyst is of course limited, since the development of an asymmetric version is not possible. Furthermore, much care has to be taken, that the iodine is the active catalyst and not traces of HI.

8 Conclusion

It has been shown that metal-free Lewis acids have been applied as catalysts in a broad variety of reactions. However, in several cases the asymmetric induction in the reactions has to be improved. While many of the highly active salts are moisture sensitive, ionic liquids with the right choice of cation and anion, are quite stable. Therefore their catalytic Lewis acidic activity is weak. The presented research field still has much room for improvement and further investigations and results are continuously reported in the literature in an increasing number due to the large potential of metal-free Lewis acids.

9 References

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Recent Advances in the Synthesis and Application of Chiral Ionic Liquids

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Abstract: The review is intended to summarize the research field of chiral ionic liquids over the last two years. Alongside the syntheses of new chiral ionic liquids, their applications are covered. Furthermore, the synthesis of task-specific ionic liquids, also known as functionalized chiral ionic liquids, and their applications are summarized.

Key words: asymmetric catalysis, asymmetric synthesis, chiral pool, ionic liquids, chirality

1 Introduction

Ionic liquids – salts which have, by definition, a melting point below 100 °C – have attracted much interest in recent years as novel solvents for reactions and electrochemical processes.[1] Some of these liquids are expected to be 'green' solvents.[2] An additional advantage is the efficient recovery of some of these salts. However, in a few examples, it is also possible that the ionic liquids are not inert and react with some reagents,[3–5] which could be a disadvantage in some applications. The range of ionic liquids based on various combinations of cations and anions has dramatically increased, and new salts[6–9] and solvent mixtures[10,11] are continuously being prepared.

Second-generation ionic liquids have been prepared from organic cations and $AlCl_x$ anions.[12] Since aluminum(III) chloride was present in these liquids, they were used as catalysts in Lewis acid catalyzed reactions. Many of the third-generation ionic liquids have also been used as solvents for catalytic reactions.[13–17] However, it is also known that third-generation ionic liquids are capable of catalyzing reactions themselves, either in substoichiometric amounts or as reaction medium.[18] Because of this relatively strong interaction[19] of the ionic liquids compared to that of other solvents, the research into various aspects of chiral solvents was renewed.

There have been several reviews about the preparation and application of chiral ionic liquids,[14,20,21] with the most recent two having been published in the middle of 2005. The presented review is intended to update the reader about the work in the field of chiral ionic liquids and functionalized chiral ionic liquids since that time.

Aside from chiral ionic liquids, there are many chiral organic salts, often with melting points over 100 °C, that have found use in organic synthesis. Compounds like chiral guanidinium salts,[22] which have been used as organocatalysts in the Michael reaction, or chiral amidinium salts,[23] which were shown to catalyze the Diels–Alder reaction with significant enantiomeric excess, could be mentioned. Asymmetric phase-transfer catalysts, which have been reviewed,[24–33] are also chiral organic salts. Furthermore, the large group of chiral nucleophilic heterocyclic carbene precursors for ligands in metal catalysis[34,35] or for carbene organocatalysts[36,37] are chiral organic salts. In some cases, these salts may have a melting point below 100 °C and can be considered to be chiral ionic liquids. However, in this review, we have collected only the work wherein the intent was to prepare and apply chiral ionic liquids.

2 Chiral Ionic Liquids

Most of the chiral ionic liquids discussed here incorporate one or more functional groups, and thus they belong to the class of functionalized chiral ionic liquids. Since the functional group is intended to perform a desired task, these functionalized ionic liquids are also referred to as task-specific ionic liquids.[1,38] Chiral ionic liquids and functionalized ionic liquids are discussed in this section.

2.1 Ionic Liquids with Chiral Cations

Amino acids are useful starting materials for ionic liquid synthesis. Guillen et al.[39] used L-histidine as a chiral precursor for the construction of a series of functionalized imidazolium-containing chiral ionic liquids, in which the chiral bifunctional unit of the amino acid remained unchanged. The first step was the formation of cyclic urea derivative **2**; this was prepared upon treatment of the histidine methyl ester dihydrochloride (**1**) with carbonyldiimidazole (CDI) without any solvent in 82% yield (Scheme 1). The reaction, carried out in *N*,*N*-dimethylformamide according to Cohen,[40] gave the product in only 74% yield.

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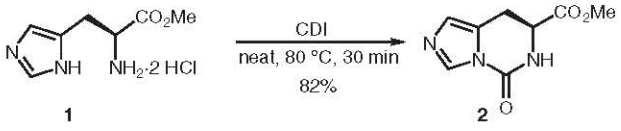
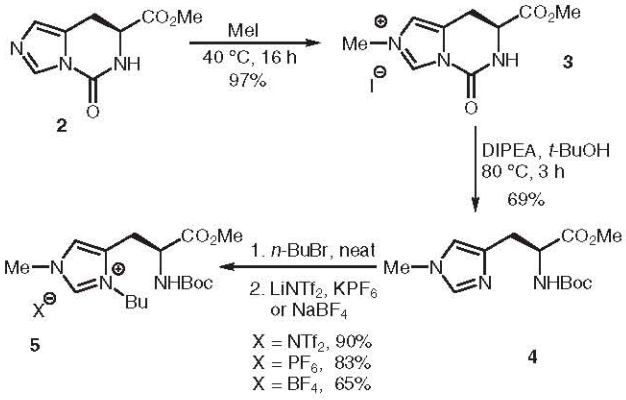


Scheme 1

Further alkylation with methyl iodide in acetonitrile gave the corresponding salt **3** in 97% yield (Scheme 2). The salt was then treated with *tert*-butyl alcohol in the presence of diisopropylethylamine, which resulted in the opened Boc-protected N-alkylated histidine methyl ester **4**. This ester was alkylated with neat *n*-butyl bromide to yield the chiral imidazolium salt **5**. Subsequent anion metathesis with lithium bistriflimide, potassium hexafluorophosphate, or sodium tetrafluoroborate gave ionic liquids which could be purified by flash column chromatography on silica gel.

The bistriflimide salt **5**, with a melting point of 46.2 °C, was also conveniently transformed into various ionic structures by means of typical methods used in amino acid



Scheme 2

chemistry (Scheme 3), including (i) deprotection, (ii) hydrolysis of the methyl ester function, and (iii) peptide coupling either at the N- or C-terminal position. Subsequent treatment of the monoprotected amino acid with *N*-Boc alanine, using O-(7-azabenzotriazol-1-yl)tetramethyluro-

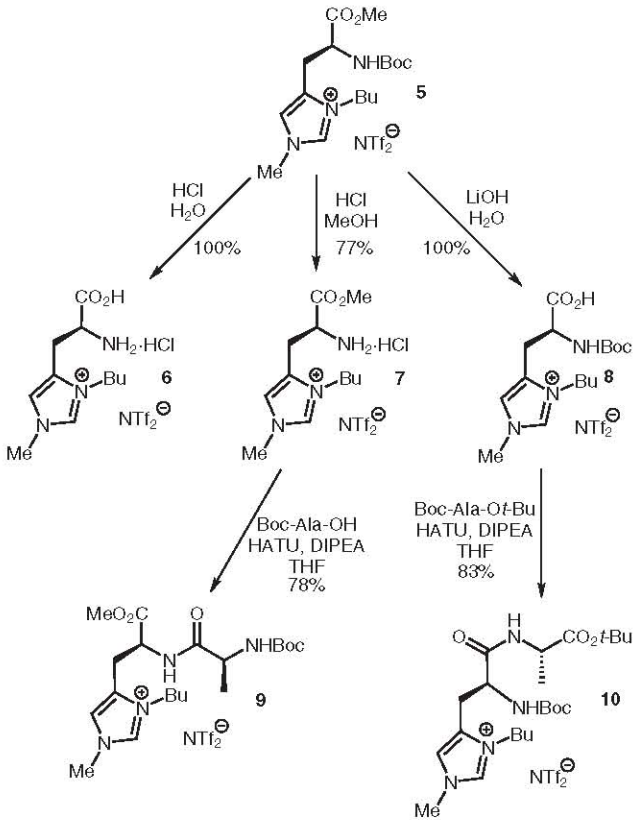
Biographical Sketches

Andreas Winkel was born in Seesen, Germany, in 1981. He started studying chemistry in 2001 at the Clausthal Technical University of Technology and began his diploma thesis in 2005 with research on the synthesis of carbon nanostructures by pyrolosis of organometallic compounds. He finished his diploma in 2006 and started his PhD thesis under the supervision of René Wilhelm. He is now working in the research field of ionic liquids with respect to chiral base-stable imidazolinium salts.

P. Vasu Govardhana Reddy was born in Proddatur, Andhra Pradesh, India in 1975. He received his MSc in chemistry at Sri Venkateswara University, Tirupati, India. He obtained his PhD in 2004 from the same university, under the supervision of Dr. C. Suresh Reddy, on the synthesis of novel phosphorus heterocyclic compounds. He then worked as a postdoctoral fellow (2004–2006) at the National Taiwan University, Taiwan under the guidance of H.-T. Chang and S.-T. Chen on the synthesis of conjugated benzothiazoles and sugar-linked paclitaxel derivatives. Currently he is working as an Alexander von Humboldt Postdoctoral Fellow at the Clausthal University of Technology, Germany under the supervision of Prof. Dr. René Wilhelm on asymmetric metal-free catalysis.

René Wilhelm was born in Hanover, Germany, in 1972. He started studying chemistry in 1993 at the University of Hanover and finished his diploma work in 1998 under the supervision of Prof. Butenschön. In 2001 he finished his PhD work, which concentrated on the chemistry of arenetricarbonylchromium complexes at Imperial College, London, in the group of Dr. Widdowson. He then obtained a position as a Feodor Lynen Postdoctoral Fellow of the Alexander von Humboldt Foundation in the group of Prof. Vollhardt at the University of California at Berkeley, USA, working on the solid-state synthesis of carbon nanotubes. After a half-year postdoctoral stay in the group of Prof. Magnus at the University of Texas at Austin, USA, he started his independent research as a Junior Professor at the Clausthal University of Technology, Germany, in 2003. His research interests are in the fields of carbon nanomaterials, catalysis and ionic liquids.

nium hexafluorophosphate (HATU) as the coupling agent in the presence of diisopropylethylamine (DIPEA), afforded the dipeptide **9** in good yield. Further applications of the obtained salts were not reported.

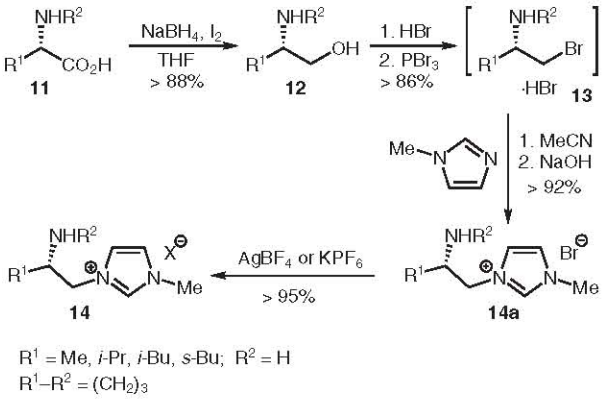


Scheme 3

Erker and co-workers had earlier reported analogues of **5** that incorporated, on both nitrogen atoms of the imidazolium ring, either propyl, isopropyl or ethyl groups.[41]

Chiral imidazolium salt ionic liquids based on an amino acid side-chain were reported by Xu and co-workers (Scheme 4).[42] The starting materials were natural amino acids like L-alanine, L-valine, L-leucine, L-isoleucine, and L-proline. These were reduced to the corresponding amino alcohols, then treated with tribromophosphine to yield the amino bromide hydrobromides. Subsequent reaction with *N*-methylimidazole led to chiral imidazolium bromides and successive anion metathesis to the corresponding tetrafluoroborate and hexafluorophosphate salts. The bromide salts all possessed melting points above 100 °C, whereas the tetrafluoroborates were all room-temperature ionic liquids. The hexafluorophosphate melting points ranged from 6 °C to 73 °C.

Ionic liquid **14** (R^1 = *i*-Pr, R^2 = H, X = BF_4) was tested for its chiral discrimination ability with racemic Mosher's acid. A downfield shift (5.91 ppm) of the racemic acid's CF_3 signal was observed with a splitting of J = 34.998 Hz. This clearly confirmed the existence of a strong diastereomeric interaction.



Scheme 4

Kou and co-workers[43] synthesized amino acid based ionic liquids upon reaction of L-proline with nitric acid, or upon anion metathesis from amino acid ester chlorides with silver nitrate or sodium saccharin (Figure 1). All reported salts were either white solids with melting points below 100 °C, or viscous oils at room temperature.

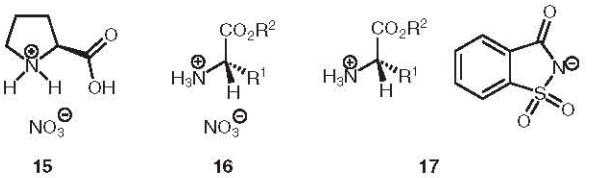
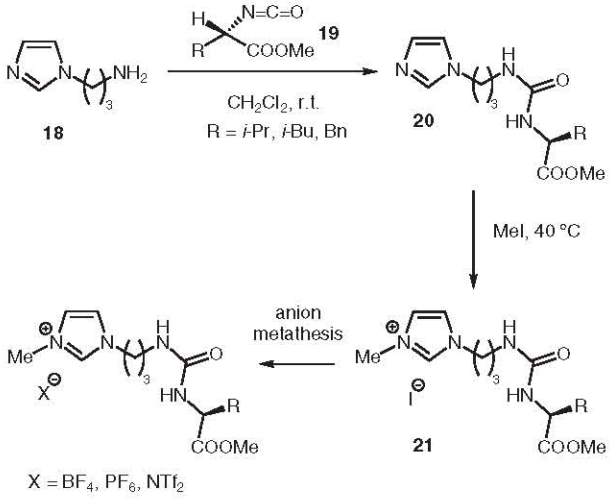


Figure 1

In addition, the amino acid ester ionic liquids were tested as chiral reaction media for the Diels–Alder reaction of cyclopentadiene to methyl acrylate (in analogy to Scheme 10). The stereoselectivities (*endo*/*exo* = 3:1 to 4:1) were comparable to those obtained in [bmim][BF_4].[44] An increase in the amount of amino acid ester from 30 mol% to 100 mol% only caused a small change in the *endo*/*exo* ratio. Saccharine ionic liquids had better stereoselectivities than the nitrates. Catalytic activity was also found in $AlaC_1NO_3$; however, the enantiomeric excess was less than 3%.

Ni and Headley[45] reported that the urea unit can be introduced into the imidazolium cation for the synthesis of chiral functionalized ionic liquids. 1-(3-Aminopropyl)-1*H*-imidazole (**18**) was treated with substituted (–)-(*S*)-2-isocyanato-3-methylbutyrate (**19**), originating from the amino acid, to yield the desired urea derivatives **20** with excellent yields (95–97%). In order to perform the alkylation, compound **20** was heated with one equivalent of iodomethane at 40 °C, neat, for 24 hours. The next step of the synthesis involved an anion metathesis of imidazolium iodide salt **21** by tetrafluoroborate, hexafluorophosphate and bistriflimide anions as shown in Scheme 5. Applications of these products have not been reported so far.



Scheme 5

Similarly, the same research groupd synthesized urea-functionalized chiral pyridinium ionic liquids from 2-(aminomethyl)pyridine and amino acid ester derived isocyanates (Figure 2).[46]

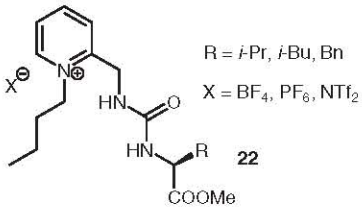
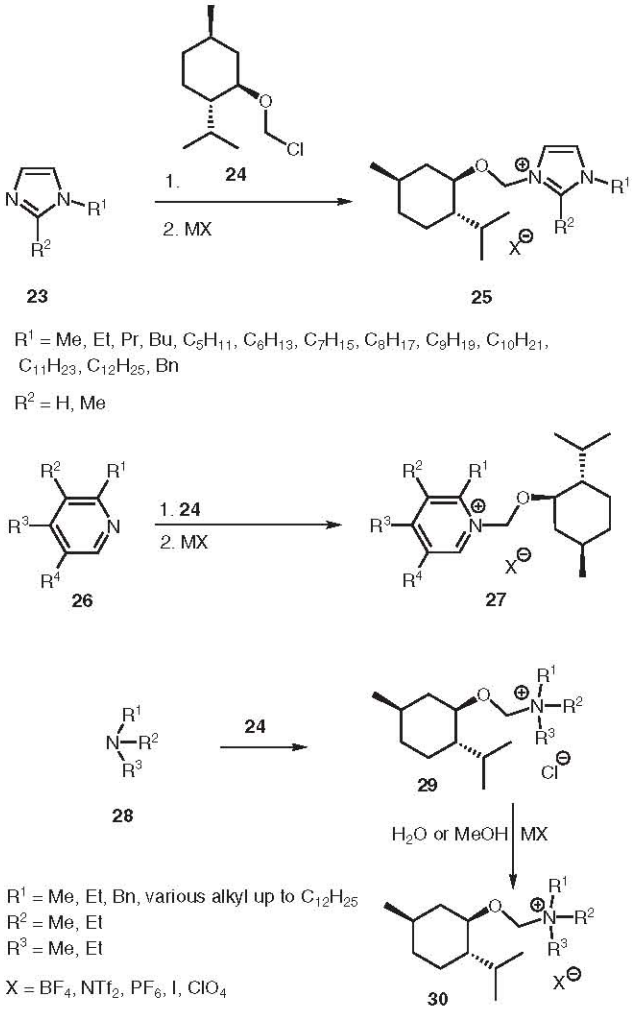


Figure 2

Terpenes and related compounds have also been used for the synthesis of chiral ionic liquids. A common step in the synthesis of chiral ionic liquids is the nucleophilic substitution reaction of an achiral nitrogen-containing nucleophile with a chiral electrophile. An important example of such an electrophile is chloromethyl (–)-(1*R*,2*S*,5*R*)-menthyl ether (**24**), which led to the corresponding chlorides **25** upon reaction with nitrogen nucleophiles like imidazoles (Scheme 6).[47]

A large number of the thus-obtained chloride salts themselves possessed ionic-liquid characteristics since their melting points were well below 100 °C. Furthermore, the chiral imidazolium chlorides were tested for antimicrobial activity against rods, cocci, and fungi. Depending on the alkyl-substituent chain length, the chlorides could be divided into (i) not active ($R^1 < C_5H_{11}$), (ii) active ($C_5H_{11} < R^1 > C_9H_{19}$), and (iii) super active ($R^1 > C_8H_{17}$).???

Subsequent to the synthesis of these chlorides was their anion metathesis with inorganic salts like potassium tetrafluoroborate, sodium perchlorate, potassium iodide, sodium hexafluorophosphate or lithium bistriflimide, or salts containing organic anions like potassium acesulfamate or the sodium salt of trifluoroacetic acid. However, the synthesized salts incorporating an iodide or hexafluo-



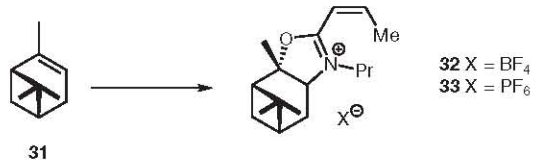
Scheme 6

rophosphate anion melted around 130 °C and therefore cannot be considered as ionic liquids. The ionic liquids based on the bis(trifluoromethanesulfonyl)imides were all room-temperature ionic liquids with viscosities ranging from 302 to 580 mm^2s^{-1} depending on the group at the 3-position of the imidazole. The synthesized salts based on the other anions possessed melting points ranging from 20 °C to 99 °C.

A second class for this type of reaction procedure was reported for substituted pyridines (Scheme 6).[48] However, the prepared pyridinium salts containing perchlorate, iodide and hexafluorophosphate as anions had melting points well above 100 °C and just a few chlorides and tetrafluoroborates possessed melting points below 100 °C. Three chiral ionic liquids **27** based on pyridinium bis(trifluoromethanesulfonyl)imides had very low melting points. For $R^1 = R^2 = R^3 = R^4 = H$, a melting point of –33 °C was found, along with a viscosity of 550 mm^2s^{-1}. When R^1 = Me and $R^2 = R^3 = R^4 = H$, the melting point was –31.4 °C and the viscosity 839 mm^2s^{-1}. With R^3 = *t*-Bu and $R^1 = R^2 = R^4 = H$, the melting point was –23.2 °C and the viscosity 1003 mm^2s^{-1}.

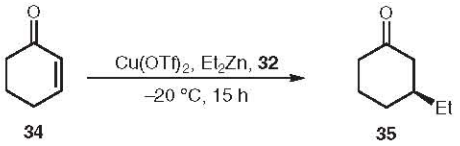
The same authors also synthesized chiral ammonium-based ionic liquids, starting from trialkylamines, following the quaternization procedure as described above (Scheme 6).[49] The melting points for salts **30** ranged from 31 °C to 150 °C. Salts incorporating a bistriflimide anion were all liquids at room temperature with viscosities ranging from 714 to 876 mm^2s^{-1}.

Other chiral sources for ionic liquid synthesis are terpenes. Malhotra and Wang[50] synthesized chiral ionic liquids based on α-pinene in 84% (**32** with BF_4) and 88% (**33** with PF_6) yield from the corresponding bromide salts via ion exchange (Scheme 7).



Scheme 7

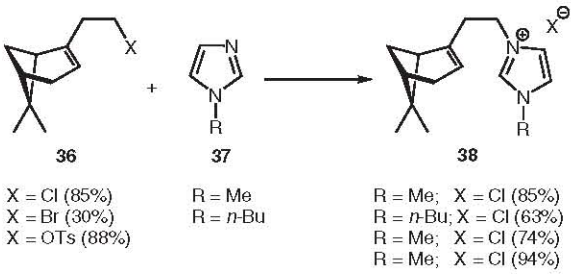
Salt **32** was tested as a chiral reaction medium in the copper-catalyzed enantioselective 1,4-addition of diethylzinc to enones (Scheme 8). The enantioselectivities obtained were moderate to good. The best result, with 90% yield and 76% ee, was found with cyclohex-2-enone (**34**) as the starting material and salt **32** with tetrafluoroborate as the counter anion. A strong influence by the achiral anion was found. When salt **33** with a hexafluorophosphate anion was used in the reaction, a similar yield of 87% was found, but the ee had decreased significantly to 35%.



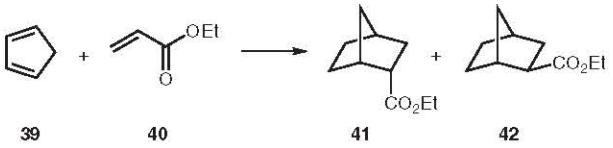
Scheme 8

Another series of chiral imidazolium ionic liquids, containing the (–)-(1*R*)-nopyl group, that is the (–)-(1*R*)-6,6-dimethylbicyclo[3.1.1]hept-2-ene-2-ethyl moiety, was recently reported. The synthesis started with the transformation of the hydroxy group into a chloride, bromide or tosylate **36**. Subsequent reaction with 1-alkylimidazole **37** led to chiral imidazolium salts **38** (Scheme 9).[51]

Further anion metathesis from the chloride salts yielded the hexafluorophosphate, nitrate, triflate, (–)-(*R*)-mandelate, and (+)-(*S*)-mandelate salts. All compounds were yellow or yellow-brown viscous liquids, except for the chloride salt bearing an *n*-butyl group at the nitrogen in the 3-position. The latter was a beige solid with a melting point of 64–67 °C. Some of the synthesized ionic liquids



Scheme 9



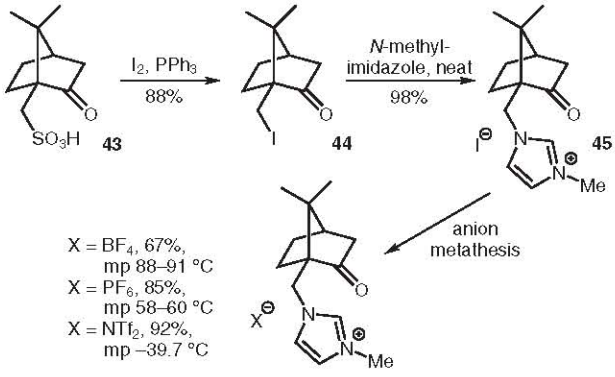
Scheme 10

were tested in the model Diels–Alder reaction of ethyl acrylate (**39**) and cyclopentadiene (**40**) (Scheme 10).

The *endo*/*exo* ratios were around 3.6:1 and thus were in the same range as those in typical organic solvents or water. The obtained products were racemic.

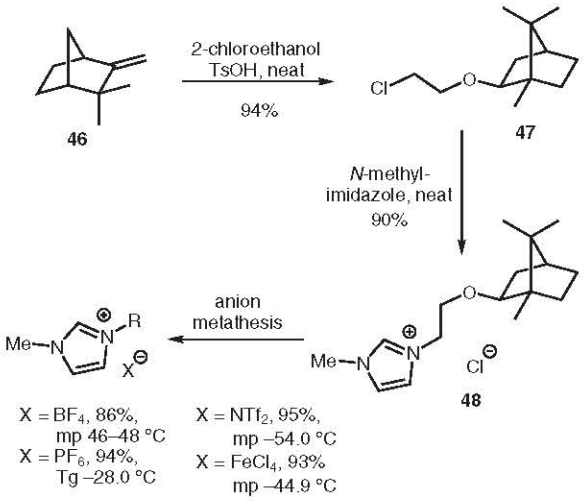
The influence of selected ionic liquids on the germination and early stages of growth and development of land superior plants (spring barley and common radish) was investigated. Concentrations of 1 and 10 milligrams ionic liquid per kilogram of soil showed no difference in comparison with control soil, whereas 100 milligrams of ionic liquid per kilogram of soil decreased the fresh weight of sprouts by around 20% for both plants tested.

Another important chiral terpene is camphor. Camphor-derived chiral imidazolium ionic liquids were synthesized by Gaertner and co-workers.[52] Treatment of (+)-(*S*)-camphorsulfonic acid with iodine and triphenylphosphine led to 10-iodocamphor. This was treated with *N*-methylimidazole to give the corresponding iodide salt, which itself was transformed into the corresponding tetrafluoroborate, hexafluorophosphate, and bistriflimide salts through ion exchange (Scheme 11).



Scheme 11

The synthesis of imidazolium ionic liquids based on a borneol unit from (+)-camphene was also reported in their work. Camphene was treated with chloroethanol under acidic conditions; this led to a Wagner–Meerwein rearrangement and to the formation of chloroethoxyborneol, which was subsequently treated with *N*-methylimidazole. Anion metathesis from the obtained chloride salt led to the ionic liquids shown in Scheme 12.



Scheme 12

However, the quaternization step in both procedures was quite time-consuming, therefore microwave heating was used to improve the reaction time and yield. For the first reaction procedure, a hold time of 45 minutes and a temperature of 130 °C gave the best result, whereas for the reaction of *N*-methylimidazole with chloroethoxyborneol, 105 minutes and 150 °C were ideal. The prepared ionic liquids were also tested as chiral reaction media in the Diels–Alder reaction of acrylic acid with cyclopentadiene. The products were obtained in racemic form.

The application of sugars like glucose derivatives, which are bio-renewable sources, as starting materials for the synthesis of chiral ionic liquids was reported by Malhotra and co-workers.[53] Novel bis(ammonium) chiral ionic liquids derived from isomannide were prepared.

D-Isomannide, also known as (1*R*,4*R*,5*R*,8*R*)-2,6-dioxabicyclo[3.3.0]octan-4,8-diol, reacted with *p*-toluenesulfonyl chloride in the presence of pyridine to yield the mono- and ditosylated derivatives. The former was used for the synthesis of monoammonium chiral ionic liquid **49** (Figure 3).

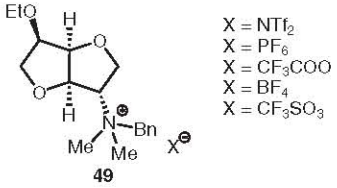
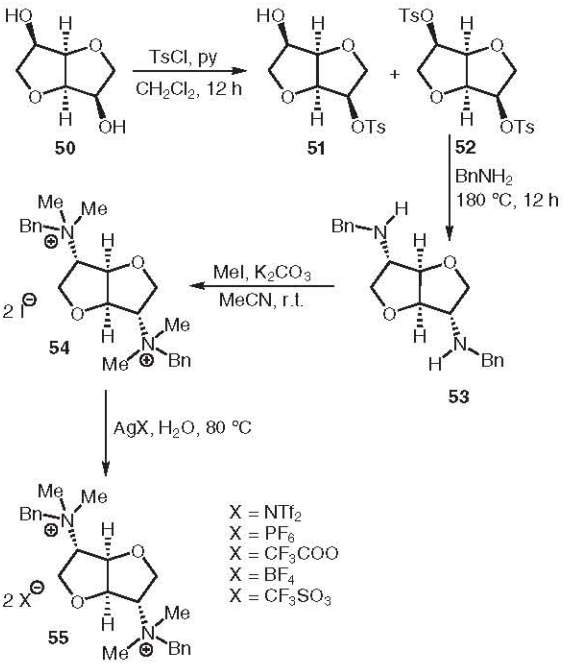


Figure 3

The ditosyl derivative was subsequently treated with benzylamine in an S_N2 reaction with inversion of configuration at the tosylate-bearing carbon atoms. The reaction had to be carried out above 165 °C to avoid incomplete substitution and concurring elimination reactions (Scheme 13).

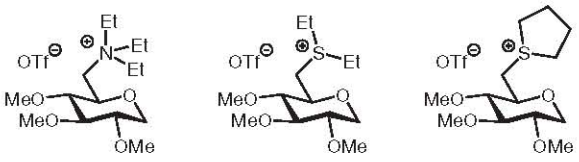
The quaternization of the bis-secondary amine was achieved by using methyl iodide with potassium carbonate as a base in acetonitrile as the solvent. The successive anion metathesis gave the chiral salts shown in Scheme 13, of which the salts containing the bistriflimide, trifluoroacetate, and triflate anions possessed melting points of 60 °C, 65 °C, and 75 °C, respectively. The other salts had melting points far above 100 °C. All salts were tested for their chiral recognition ability (that is, their diastereomeric interaction with racemic Mosher's acid silver salt). High splitting of the CF_3 signals was observed; the salts showed excellent interaction that was also dependent on the anion used.



Scheme 13

Glucose itself is a low-cost source for chiral solvents. Poletti et al.[54] used methyl α-D-glucopyranoside as a starting point for the synthesis of the three salts shown in Figure 4, of which **57** is a room-temperature ionic liquid. Both **56** and **58** are chiral triflate salts with melting points at 137.5 °C and 110 °C, respectively.

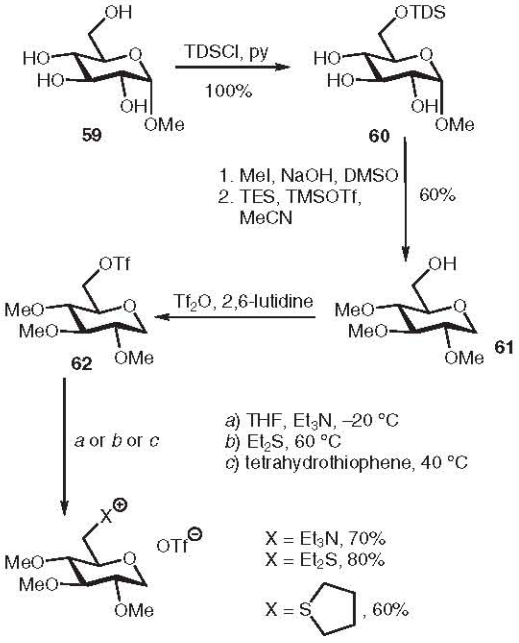
The reaction of the glucopyranoside with thexyldimethylchlorosilane (TDSCl) in the presence of pyridine afforded the silylated product in quantitative yield (Scheme 14). The reactive secondary hydroxy groups were then protected with methyl iodide in the presence of sodium hydroxide. Subsequent reduction of the anomeric position was achieved with triethylsilane and trimethylsilyl trifluoromethanesulfonate in 60% yield. Triflic anhydride was



56 57 58

Figure 4

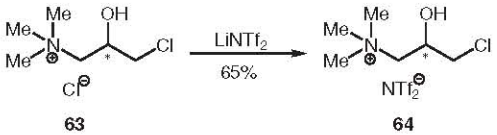
used in order to transform the primary hydroxy group into the corresponding triflate. This triflate was purified rapidly through flash-column chromatography and was used as such without any further purification. The final step was the nucleophilic attack of triethylamine, diethyl sulfide, or tetrahydrothiophene at the triflate-bearing carbon atom.



59 60 61 62

Scheme 14

Several readily available commercial sources give very easy access to ionic liquids. Tran et al., for example, used commercially available (*R*)- and (*S*)-[(3-chloro-2-hydroxypropyl)trimethylammonium] chloride salts (**63**) to prepare the enantiomerically pure bistriflimide salts **64** by simple anion metathesis (Scheme 15).[55]



63 64

Scheme 15

The chloride, tetrafluoroborate, and hexafluorophosphate salts of **63** were all solids at room temperature. This demonstrated again the importance of the anion. In addition, the ionic liquids were stable up to 300 °C and did not racemize upon heating, at least not up to the tested 150 °C region. This meant that the ionic liquids could be suitable as chiral stationary phases for gas chromatography and as chiral solvents for high-temperature reactions. The enantiomeric recognition ability was tested with racemic Mosher's acid sodium salt. Facile differentiation of the chiral (*S*)-IL **64** was found with the *R*-configured Mosher's salt. The difference in the fluorine signals was found to be 24.6 Hz. The same research group also showed that this salt was valuable for the determination of enantiomeric purity of drugs.[56]

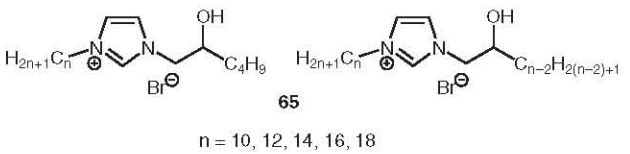
The chiral ionic bistriflimide salts of ethylcholine and phenylcholine were evaluated as additives to cyclodextrins for enantioselective separations by capillary electrophoresis.[57] It was found that the chiral ionic liquids did not induce direct enantioselectivity.

The chiral ionic liquids prepared from (*S*)- and (*R*)-phenylethylamine both showed chiral discrimination with racemic Mosher's salt.[58]

Chiral ammonium-based ionic liquids with a hydroxy group were recently prepared from isosorbide,[59] and were tested in an asymmetric aza-Diels–Alder reaction.[60]

Salts containing an appended hydroxy group based on imidazolium cations have been synthesized.[61–69] The known salt (*S*)-3-ethyl-1-(1-hydroxypropan-2-yl)-1*H*-imidazol-3-ium hexafluorophosphate[70] was recently applied in an intramolecular 1,3-dipolar cycloaddition which led to the formation of a single diastereomer.[71]

Recently, Lin and co-workers prepared a new class of ionic liquids using epoxides for the introduction of a hydroxy-bearing *N*-alkyl group (Figure 5).[72] Two different synthetic methods were followed (Scheme 16). The first procedure involved the generation of 1-(2-hydroxyalkyl)imidazole from the reaction of imidazole with an appropriate 1,2-epoxyalkane. Subsequent reaction with alkyl bromide produced the desired bromide salts. The second method produced the 1-alkylimidazole first, and this was then treated with the 1,2-epoxyalkane. However, this second method mainly provided mixed imidazolium salts which gave rise to a number of separation problems. In addition, yields were low when long alkyl groups were present on the starting epoxide.

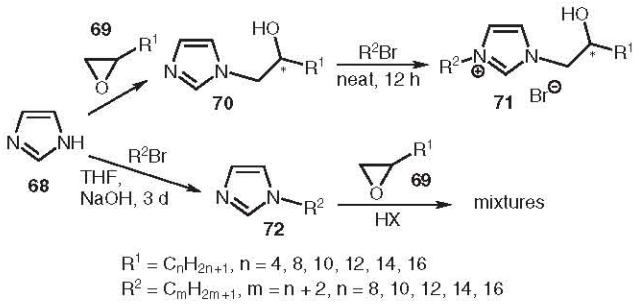


65

n = 10, 12, 14, 16, 18

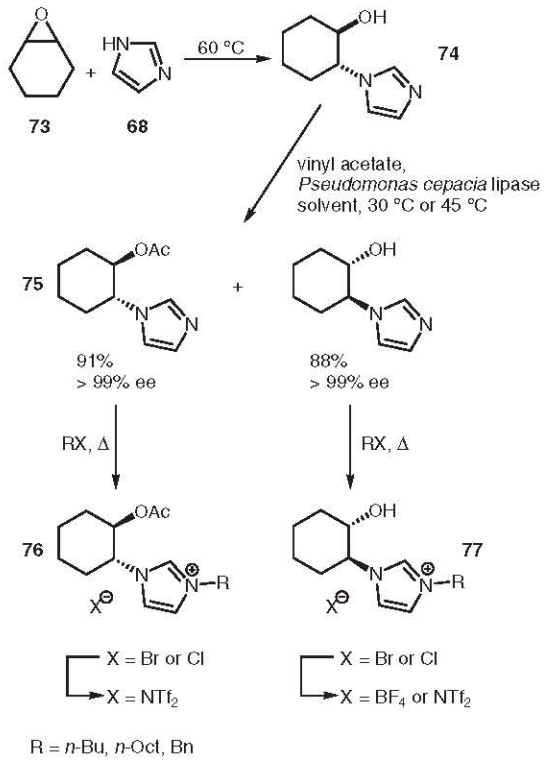
Figure 5

The obtained compounds **71** had relatively low melting points, but high clearing temperatures. A few salts with shorter chains showed a tendency to form room-temperature ionic liquids with clearing temperatures up to 185 °C.



Scheme 16

One synthesis of novel enantiopure ionic liquids made use of an efficient enzymatic resolution of (±)-2-(1*H*-imidazol-1-yl)cyclohexanol.[73] The cyclohexanol was prepared by reaction of imidazole with 7-oxabicyclo[4.1.0]heptane (Scheme 17).[74] Subsequent O-acylation with vinyl acetate took place smoothly in the presence of an enzyme. The enzyme and solvent system most efficient for the resolution was *Pseudomonas cepacia* lipase in methyl *tert*-butyl ether; this gave an excellent enantioselectivity ($E > 200$) after reaction at 45 °C for 15 hours. Under these conditions, the enantiomeric excesses of the obtained *R*,*R*-configured O-acylated product and the *S*,*S*-configured starting material were found to be >99%. The isolated yields were 91% and 88%, respectively, based on 50% theoretical yields. Both compounds were then treated with various electrophiles to yield bromide or chloride salts which themselves were transformed into bis(trifluoromethanesulfonyl)imides upon anion metathesis with lithium bistriflimide.

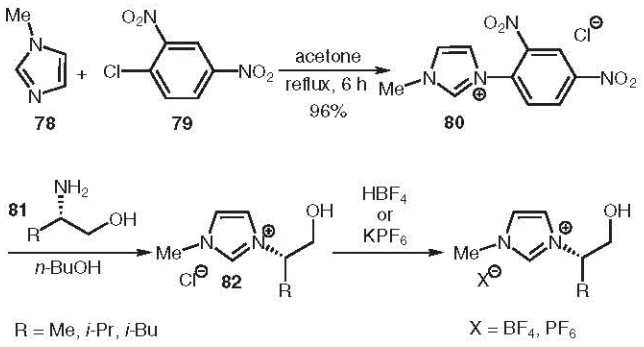


Scheme 17

Except for those bearing a benzyl group with a bromide or chloride as anion, the salts **76** and **77** were all room-temperature ionic liquids. Thermogravimetric analysis was used to test their thermal stability. A weight loss of less than 5% was observed for the bistriflimide derivative for temperatures below 20 °C. Applications of these salts were not reported.

Common building-blocks for ionic liquids are chiral amino alcohols, which can be obtained via reduction from the corresponding enantiopure amino acids. These amino alcohols played, for example, an important role in the synthesis of chiral imidazolium ionic liquids for introducing the hydroxyalkyl group onto the imidazolium moiety.[75]

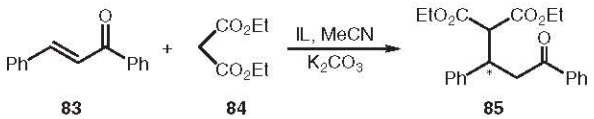
N-Methylimidazole (**78**) was treated with 1-chloro-2,4-dinitrophenylbenzene (**79**) in acetone to yield the desired imidazolium chloride **80**. Reaction with enantiopure amino alcohols **81** gave methyl hydroxyalkylimidazolium chlorides **82** which are room-temperature ionic liquids. Anion metathesis with tetrafluoroboric acid or potassium hexafluorophosphate led to the corresponding tetrafluoroborate and hexafluorophosphate salts, respectively. These had higher melting points than the chlorides, but they were still well below 100 °C (Scheme 18).



Scheme 18

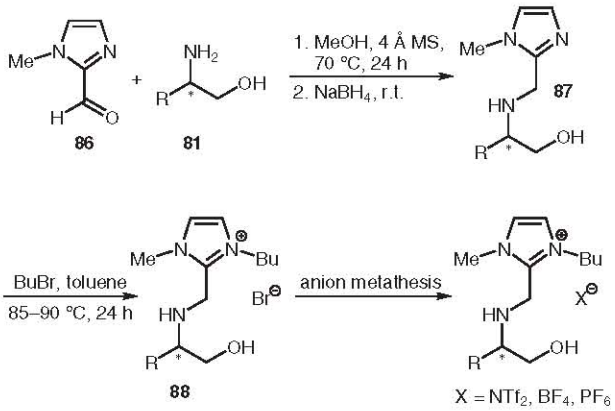
Besides the synthesis itself, the authors reported the testing of the ionic liquids **82** as chiral reaction media for the enantioselective Michael addition of diethyl malonate (**84**) with chalcone (**83**) in the presence of potassium carbonate and acetonitrile as a cosolvent (Scheme 19). Yields were in the range of 52% to 86%, with long reaction times of three to five days. The chloride salts gave lower yields than the borates and phosphates. The enantiomeric excess was determined by optical rotation measurements and varied between 0% and 15% ee.

A reaction procedure where the amino alcohol moiety was introduced at the C2-position of a carbonyl-bearing alkylimidazole was developed by Headley and co-workers



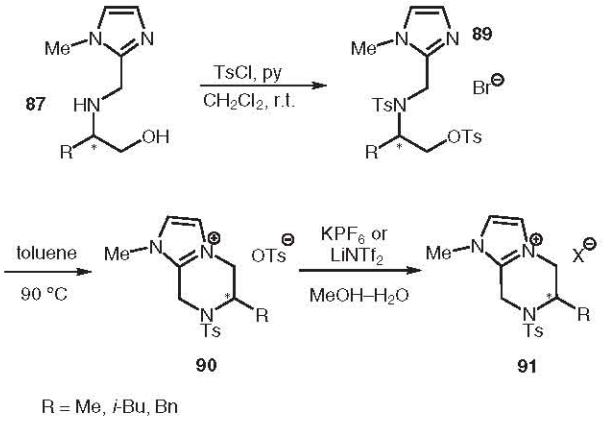
Scheme 19

(Scheme 20).[76] 1-Methyl-1*H*-imidazole-2-carbaldehyde (**86**) reacted with enantiopure amino alcohols **81** to give the corresponding Schiff's base precursors which were subsequently reduced with sodium borohydride. The obtained imidazole derivatives **87** were then quaternized with bromobutane in toluene to give the corresponding bromide salts **88**. Anion metathesis led to the tetrafluoroborate, hexafluorophosphate, and bistriflimide salts.



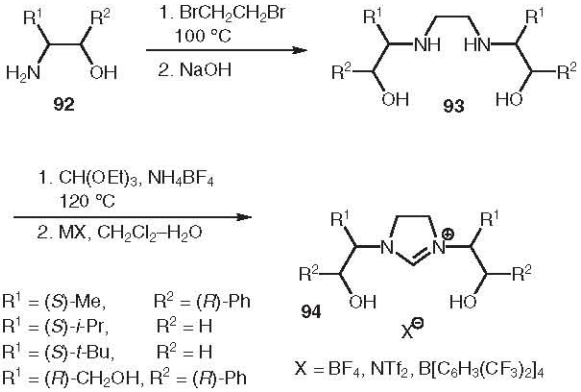
Scheme 20

The preparation of a novel set of imidazolium ionic liquids, also with a chiral moiety at the 2-position of the imidazolium cation, is related to the synthesis described above.[77] The first step was similar and yielded the chiral imidazole derivates **87** (Scheme 21). Subsequent reaction with tosyl chloride in the presence of pyridine in dichloromethane led to the formation of the N- and O-tosylated products **89**. For ring closure to occur, compounds **89** were heated in toluene, thus affording the desired tosylate salts in excellent yield. Anion metathesis led to the hexafluorophosphate and bistriflimide salts. To confirm the successful ring closure, X-ray crystallographic analysis was carried out on **90**. Furthermore, the acidity of the CH_2 position adjacent to the 2-position of the imidazolium cation was probed. Under neutral conditions in D_2O, deprotonation did not occur; deprotonation did, however, take place in basic media that contained triethylamine.



Scheme 21

Chiral ionic liquids based on an imidazolinium cation containing two hydroxy groups, specifically 4,5-dihydroimidazolium, were prepared from amino alcohols in two steps, as shown in Scheme 22.[78] The salts had melting points between 100 °C and room temperature and were capable chiral shift reagents with racemic Mosher's salts.

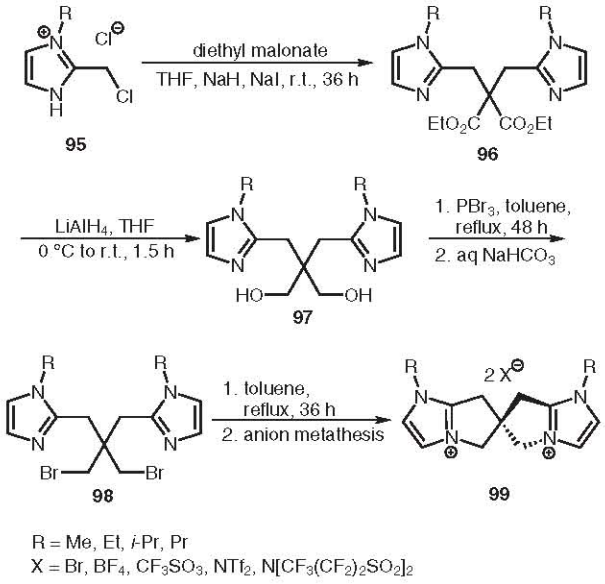


Scheme 22

Novel chiral imidazolium salts **99**, with a spiro skeleton were synthesized in racemic form by Sasai et al. (Scheme 23).[79] The synthesis of symmetrical spiro-imidazolium salts started with the alkylation of diethyl malonate with imidazolium salt **95** and was followed by reduction with lithium aluminum hydride to afford the corresponding diol **97**. This was transformed into a dibromide upon reaction with tribromophosphine. The N-alkylation (or double ring closure) took place smoothly in refluxing toluene to yield spiro-imidazolium bromide **99** (X = Br). Subsequent anion metathesis led to the tetrafluoroborate, triflate, bistriflimide, and bis(heptafluoropropanesulfonyl)imide salts, respectively. The bromide salts demonstrated a diastereomeric interaction with (*S*)-Mosher's salt. The ^{1}H NMR spectrum exhibited excellent splitting in each pair of doublets arising from the protons of the spiro skeleton.

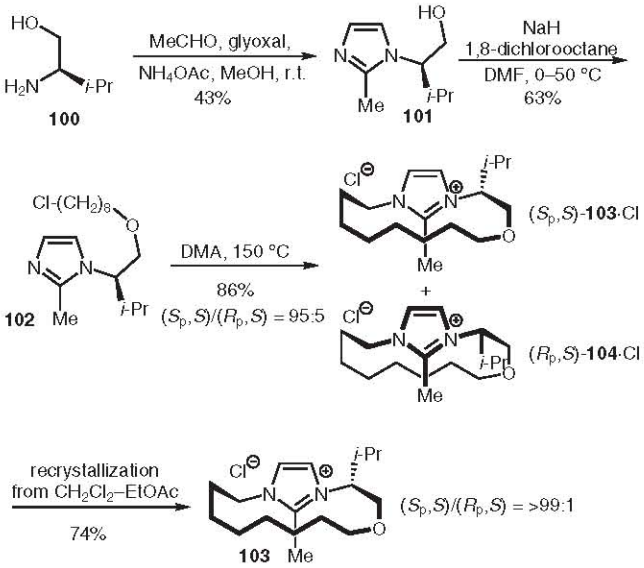
To obtain ionic liquids with low melting points, unsymmetrical spiro-imidazolium salts were also prepared. Monoalkylation of diethyl malonate with **95** was followed by the treatment with another imidazolium chloride salt **95** bearing a different alkyl group. The resulting asymmetric disubstituted malonate was reduced to afford the corresponding diol. The synthesis proceeded with the steps described above. However, the synthesis produced mainly high-melting salts and just a few ionic liquids were reported: with R = *i*-Pr, X = NTf_2, mp 68 °C; with R = *i*-Pr, X = $N[CF_3(CF_2)_2SO_2]_2$, mp –10 °C; and with R = Pr, *i*-Pr, X = NTf_2, mp –20 °C.

The chiral information in ionic liquids can also arise from planar chirality.[80] An imidazolium-based ionic liquid with cyclophane-type planar chirality was synthesized in optically pure form by Ishida and Saigo (Scheme 24).[81] The synthesis started from L-valinol with the preparation of an enantiopure imidazole bearing a chiral nitrogen substitu-



Scheme 23

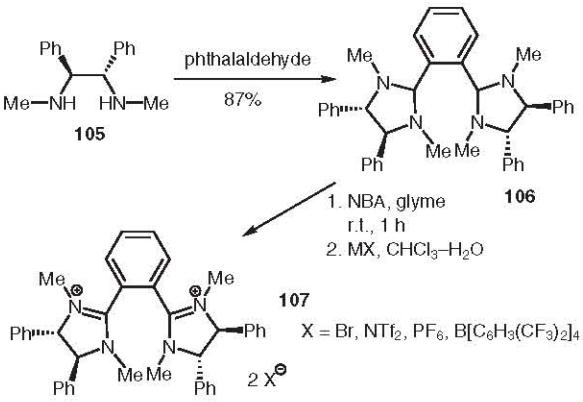
ent. Further reaction with 1,8-dichlorooctane led to the corresponding ether, then the intramolecular quaternization was carried out by heating a solution of the ether in *N*,*N*-dimethylacetamide (DMA). Two diastereomers were formed in a high diastereomeric ratio (dr = 95:5), enabling the isolation of the target material in a diastereomerically pure form; the major isomer was purified by recrystallization.



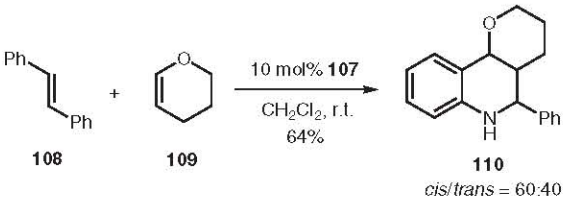
Scheme 24

Subsequent anion metathesis with bis(trifluoromethanesulfonyl)imide and 2,2,2-trifluoro-*N*-(trifluoromethanesulfonyl)acetamide led to the corresponding salts in high yields of 86% and 95%, respectively. The first was a low-melting salt (mp 53 °C), whereas the latter was a room-temperature ionic liquid with a glass transition point of –35 °C. Furthermore, the ionic liquids were successfully tested as chiral recognition agents with racemic Mosher's salt and *O*-ethyl phenylphosphonothioate, as demonstrated by ^{19}F and ^{31}P NMR spectroscopy experiments.

Chiral imidazolinium salts, that is, 4,5-dihydroimidazolium and bisimidazolinium salts, have been prepared, for example, from chiral diamines via the simple route outlined in Scheme 25.[82] The salts were found to catalyze the aza-Diels–Alder reaction of imines with Danishefsky's diene. It was shown that an increase in the lipophilicity of the counter-anion resulted in a higher reactivity.[83] In addition, salt **107** was used to catalyze the inverse-electron-demand aza-Diels–Alder reaction of dihydropyran with an imine (Scheme 26). This reaction was not sufficiently catalyzed by monoimidazolinium salts. The products were obtained as racemates. Furthermore, salt **107** was able to act as a chiral shift reagent with racemic Mosher's carboxylate as ascertained by ^{1}H and ^{19}F NMR spectroscopic analysis.



Scheme 25



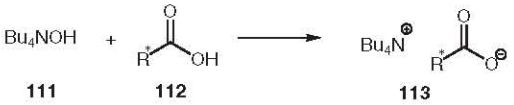
Scheme 26

Finally, in a series of ionic liquids based on hexaalkylguanidinium tetrafluoromethanesulfonates, one chiral example was presented, wherein one of the alkyl groups was (*S*)-(–)-phenylethyl.[84]

2.2 Ionic Liquids with Chiral Anions

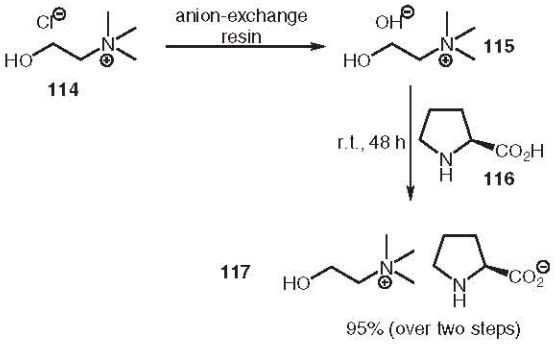
A common procedure for ionic liquid synthesis where the final ionic liquids contain chiral anions is the reaction of an achiral hydroxide salt with a chiral carboxylic acid, resulting in a simple neutralization reaction that gives water and the ionic liquid with a chiral carboxylate as the anion. The achiral hydroxide salt is often obtained from exchange of a halide by use of an ion-exchange resin.

Maschmeyer and co-workers[85] reported the facile synthesis of ionic liquids possessing chiral carboxylates. A solution of tetrabutylammonium hydroxide (**111**) was mixed with a suspension of a chiral carboxylic acid **112** and heated for two hours at 60 °C (Scheme 27). Removal of the water by distillation produced a residue which was dissolved in acetonitrile, filtered and dried over sodium sulfate. Removal of the solvent then yielded the chiral carboxylates. The range of acids used in this synthesis included typical enantiopure amino acids like L-alanine, L-phenylalanine and L-valine, as well as tartaric acid, mandelic acid and malic acid. In the end, 23 new chiral ionic liquids were prepared; all were liquid at room temperature except the [*N*-Ac-L-Cys]-derived ionic liquid which had a melting point of 42–44 °C.



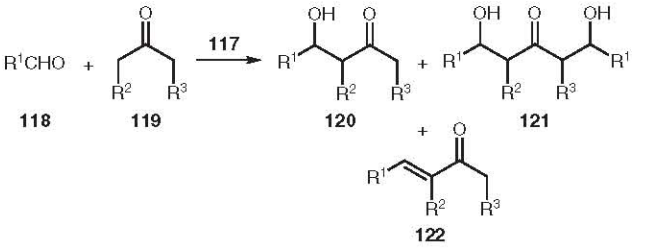
Scheme 27

A related approach was reported by Han and co-workers.[86] In this, choline chloride (**114**) was converted into the corresponding hydroxide upon treatment with an ion-exchange resin (Scheme 28). The resulting hydroxide reacted with enantiopure L-proline to yield the corresponding ionic liquid **117**, as a light yellow oil with a decomposition temperature of 159.7 °C, in 95% yield after two steps.



Scheme 28

Ionic liquid **117** was tested as a catalyst for the aldol reaction of various substituted benzaldehydes **118** to acetone, or acetone derivatives, as outlined in Scheme 29. Under solvent-free conditions the reaction was complete in a very short time. In particular, when 30 mol% of the ionic liquid was used with 4-nitrobenzaldehyde and acetone as the reactants, the reaction was instantaneous. Mainly the normal aldol product **120** and the second aldol product **121** were formed. The dehydrated product **122** was found when benzaldehyde, or benzaldehyde substituted with electron-donating groups, reacted with acetone. The observed enantioselectivities were less than 10%.

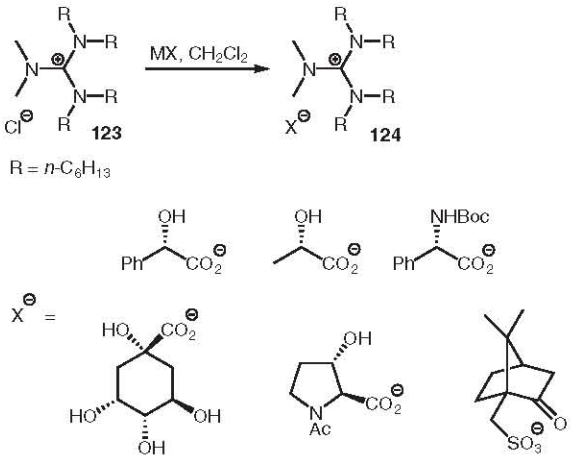


Scheme 29

A similar procedure was applied by Ohno and co-workers,[87] who prepared ionic liquids containing a tetraalkylammonium or pyridinium cation and a chiral carboxylate anion derived from L-alanine. Furthermore, the synthesis of tetrabutylphosphonium-type amino acid ionic liquids was reported. The general procedure followed that already described above. No applications were reported.[88]

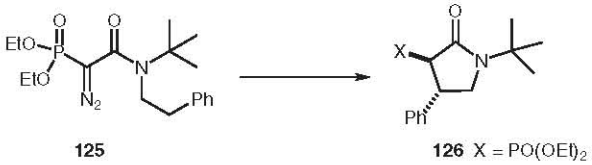
Zhao et al.[89] started with chiral or ω-amino acids and treated them with 1-ethyl-3-methylimidazolium hydroxide to afford the corresponding ionic liquids. Subsequently, the enzymatic resolution of DL-phenylalanine methyl ester was tested in the presence of the prepared ionic liquids. Moderate-to-high enzyme enantioselectivities were found. In some examples, the enantiomeric excess values were as good as those observed with pure water as solvent.

Guanidinium salts containing chiral anions were tested in rhodium(II) carbenoid asymmetric C–H insertion and in Sharpless asymmetric dihydroxylation reactions.[90] The ionic liquids were prepared by treatment of tetra(*n*-hexyl)dimethylguanidinium chloride (**123**) with readily accessible chiral anions in dichloromethane at room temperature (Scheme 30).



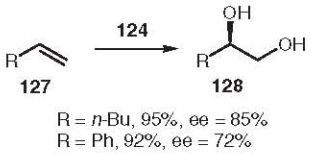
Scheme 30

Using the chiral ionic liquid containing the mandelate anion as reaction medium and rhodium acetate as a catalyst, the γ-lactam **126** was obtained in 72% yield from the diazoacetamide with a *trans*/*cis* ratio of 67:33 and an enantiomeric excess of 27% (Scheme 31).



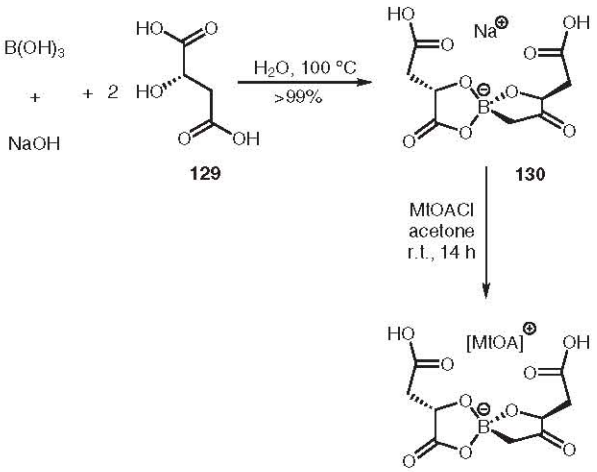
Scheme 31

For the Sharpless asymmetric dihydroxylation shown in Scheme 32, hex-1-ene and styrene were used as alkenes. The reactions were carried out in the presence of an osmium catalyst and 4-methylmorpholine *N*-oxide as co-oxidant. As reaction medium, the ionic liquid **124** with an anion derived from deprotonated quinic acid was used. The diols were obtained in high yields and high enantiomeric excesses.



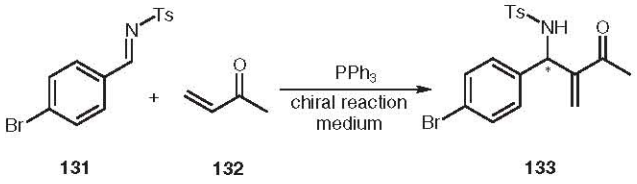
Scheme 32

Leitner and co-workers[91] prepared a methyltrioctylammonium dimalatoborate in two steps from L-malic acid. First, sodium dimalatoborate **130** was prepared, and then was converted into the product ionic liquid upon ion exchange in acetone (Scheme 33).



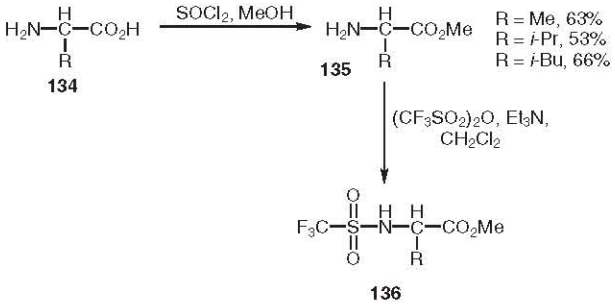
Scheme 33

The chiral liquid was tested as a reaction medium in the aza-Baylis–Hillman reaction of methyl vinyl ketone (**132**) and *N*-(4-bromobenzylidene)-4-toluenesulfonamide in the presence of triphenylphosphine (Scheme 34). Conversions varied between 34% and 39% and the enantioselectivity ranged from 71% to 84% ee.



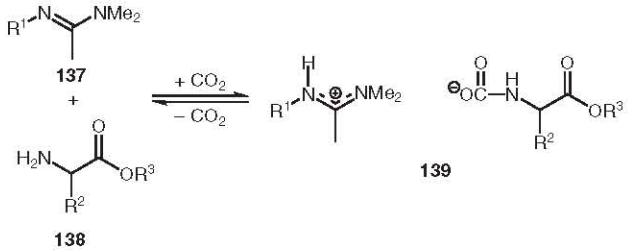
Scheme 34

Chiral ionic liquids based on a chiral triflimide derivative were prepared by Fukumoto and Ohno (Scheme 35).[92] The first step involved the esterification of enantiopure amino acids **134** to yield the amino acid methyl ester hydrochlorides. Subsequent reaction with trifluoromethanesulfonic anhydride in the presence of triethylamine in dichloromethane led to the corresponding *N*-trifluoromethanesulfonyl amino acid methyl esters **136**. The final ionic liquids were prepared upon neutralization reaction of [bmim]$^-$ and tetrabutylphosphonium hydroxide with the amino acid derivative. All salts were room-temperature ionic liquids.



Scheme 35

Ionic liquids containing chiral anions were also produced in the reaction of amidines and amino acid esters with carbon dioxide (Scheme 36);[93] this was carried out by bubbling of carbon dioxide through the mixture of amidine and amino ester. The mixture had to be cooled in a water bath since the uptake of carbon dioxide was slightly exothermic.

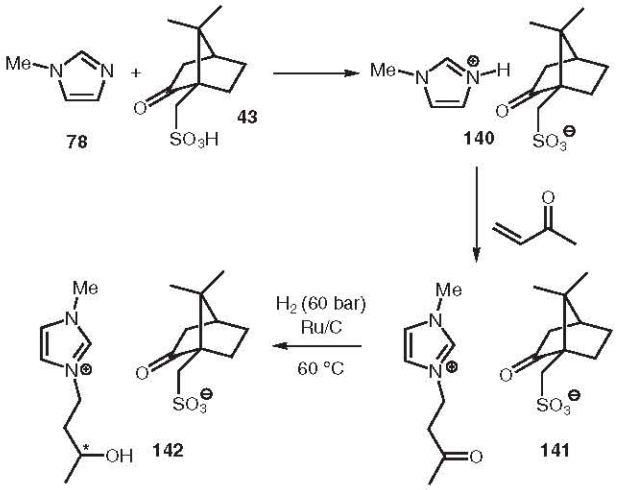


Scheme 36

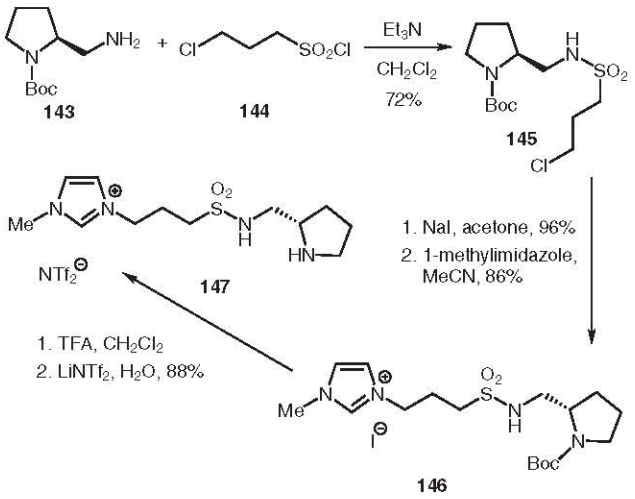
Methyl, octyl, and octadecyl amino acid esters were used for this reaction. Common amino acid ester sources were enantiopure leucine, isoleucine, valine, phenylalanine, tyrosine, and proline. The uptake of carbon dioxide was measured as a function of time. The equilibrium could be

shifted to the nonionic state when nitrogen gas was passed through the ionic liquid, or by heating above 50 °C in air.

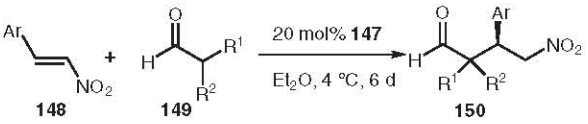
A chirality transfer in ionic liquid **141** through the help of ion-pairing was recently reported.[94] The starting chiral ionic liquid was prepared according to Scheme 37. In the hydrogenation to **142**, an enantiomeric excess of up to 80% was found.



Scheme 37



Scheme 38



Scheme 39

3 Ionic Liquid Supported Chiral Catalysts

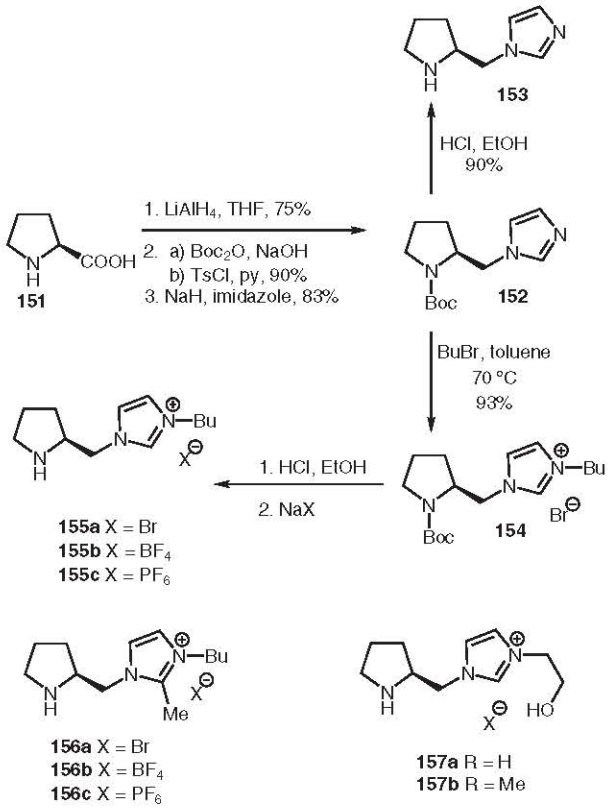
Task-specific ionic liquids, where an ionic unit is attached to a catalyst, are also called supported ionic liquid catalysts. The ionic unit functions as a support for the catalyst in order to recover it from the reaction mixture.

Recently, Headley and co-workers[95] prepared pyrrolidine-based chiral ionic liquids via the reaction of 3-chloropropanesulfonyl chloride (**144**) with *tert*-butyl (2*S*)-2-(aminomethyl)pyrrolidine-1-carboxylate (**143**)[96] to form sulfonamide **145**. The latter was converted into imidazolium iodide **146** in 86% yield in two steps, involving iodation with sodium iodide and alkylation of the corresponding pyrrolidine sulfonamide with 1-methylimidazole in acetonitrile. Finally, the chiral ionic liquid **147** was obtained after removal of the Boc group and subsequent anion metathesis to the bistriflimide in 88% overall yield (Scheme 38).

The Michael reaction of aldehydes **149** and nitrostyrenes **148** in various solvents was examined, using 20 mol% pyrrolidine-based chiral ionic liquid **147** as organocatalyst (Scheme 39). In polar solvents, such as methanol and isopropanol, the reaction proceeded smoothly and gave the desired Michael adduct in good yields (62–80%) and enantioselectivities (66–67% ee). However, when less polar solvents, like diethyl ether and chloroform, were used in conjunction with the chiral ionic liquid, the Michael adduct was obtained in only moderate yields (43–52%) but better enantioselectivities (76–78% ee). Moreover, at lower temperature (4 °C) after six days, the adduct was obtained in 82% ee and 58% yield. The catalyst could be recycled twice without loss of activity or enantioselectivity.

In 2006, the Cheng group[97] proposed a novel class of pyrrolidine-type chiral ionic liquids from L-proline (Scheme 40). All the chiral ionic liquids obtained were viscous liquids at room temperature and were soluble in moderately polar solvents, such as chloroform, dichloromethane, and methanol, but insoluble in less polar solvents, such as diethyl ether, ethyl acetate, and hexane. These properties, together with the straightforward synthesis, make these chiral ionic liquids suitable for practical applications in asymmetric synthesis.

The Cheng group investigated the use of these pyrrolidine-type chiral ionic liquids in the Michael addition of ketones to nitroalkenes in analogy to Scheme 39. The functionalized chiral ionic liquids that they tested performed much better than previously reported chiral pyrrolidine catalysts with ionic liquids as the reaction media.[98,99] For example, 40 mol% of proline was required to catalyze the addition of cyclohexanone to nitrostyrene in ionic liquids, and 75% yield was obtained only after 60 hours (dr = 95:5, with 75% ee for the *syn* diastereomer).[99] These observations, together with pyrrolidine-imidazole conjugate **153** (which is structurally similar to **155**) clearly indicated the critical role of the ionic liquid moieties for asymmetric catalysis. Overall, the pyrrolidinylimidazolium bromide and tetrafluoroborate salts, **155a** and **155b** respectively, demonstrated the best performances with nearly quantitative yields and high diastereoselectivity (*syn*/*anti* = 99:1) and enantioselectivity (98% ee). Preliminary studies showed that the chiral ionic liquids **155a** and



Scheme 40

155b could also catalyze the Michael addition of aldehydes. Under the optimized conditions, the addition of isobutyraldehyde to *trans*-β-nitrostyrene gave the desired adduct in good yields and up to 89% ee. Valeraldehyde also worked well, and afforded the desired product with quantitative yield and moderate selectivity (*syn*/*anti* = 90:10, 72% ee). The functionalized chiral ionic liquids still maintained the biphasic property of ionic liquids and was recycled by precipitation with diethyl ether. Recycled **155b** gave the product in the same time. After the third and fourth cycle the reaction time increased; however, still excellent yields and enantiomeric excess were obtained.

Xu et al.[100] reported a similar kind of chiral pyrrolidine from commercially available L-proline (Figure 6). These chiral pyrrolidine organocatalysts were then tested in the direct asymmetric Michael addition of cyclohexanone to β-nitrostyrene to afford the Michael adduct in analogy to the reaction shown in Scheme 39. The catalytic performance of **158a**,**b** was comparable to that achieved with the parent proline in the ionic liquid [bmim][PF_6]. Catalysts **159a**,**d** also gave moderate to good enantioselectivities. Significantly, the **158b**-catalyzed Michael addition proceeded smoothly in [bmim][PF_6] to give adduct **5** in much higher yield (98%) and much better enantioselectivity (97% ee) than obtained from the use of conventional organic solvents like dimethyl sulfoxide, *N*,*N*-dimethylformamide and isopropanol. The lower efficiency of **158b** in molecular organic solvents indicated the importance of a synergistic effect in the catalytic system of ion-supported pyrrolidine-[bmim][PF_6]. Various aromatic-substituted nitroalkenes reacted smoothly and the yields were generally good, though the type of substrate appeared to influence the enantioselectivity of the reaction. β-Nitroalkenes substituted with an electron-donating group and aromatic nitroalkenes without substituents were found to be excellent Michael acceptors to give products with high enantioselectivities (up to 99%), while β-nitrostyrenes with an electron-withdrawing group, linear ketones, and aldehydes provided the desired adducts in moderate enantioselectivities.

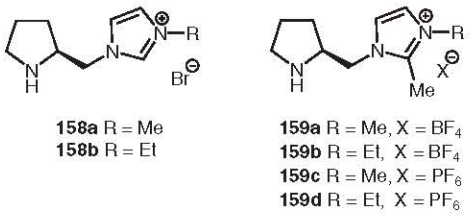
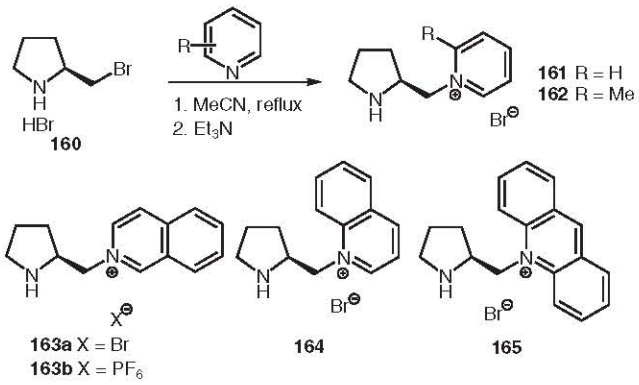


Figure 6

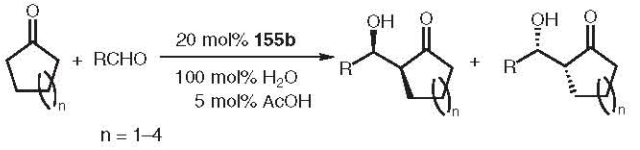
Xu et al.[101] also synthesized a novel class of pyrrolidinyl pyridinium bromides **161**–**165**. These were readily prepared by treatment of pyridine or pyridine derivatives with (+)-(*S*)-2-bromomethylpyrrolidine hydrobromide (**160**).[42,100] Anion metathesis of **163a** with potassium hexafluorophosphate afforded **163b** (Scheme 41). Organocatalysts **161**–**165** were demonstrated to efficiently catalyze the asymmetric Michael addition reactions of unmodified cyclohexanone to nitroalkenes in the ionic liquid [bmim][BF_4] with up to 95% yield and nearly 100% ee.



Scheme 41

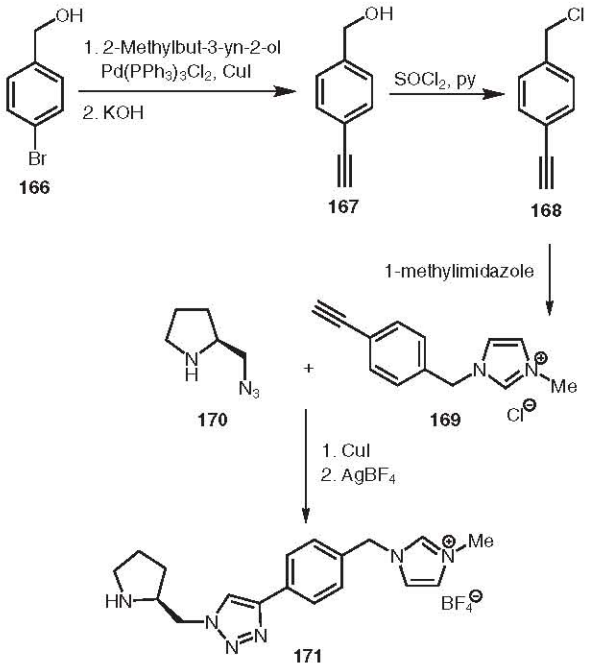
In addition to their investigation of the application of salt **155b** to the asymmetric Michael addition, Cheng and coworkers[102] also evaluated the use of **155b** in the asymmetric aldol reaction. In their study, the synthetic functionalized chiral ionic liquid **155b** was tested with cyclic ketones and aldehydes, and the reactions generated the desired aldol products in high yields and moderate enantioselectivities (Scheme 42). The recyclability and reusability of functionalized chiral ionic liquid catalysts were examined for the reactions of cyclopentanone and

o-nitrobenzaldehyde, with **155b** as the representative catalyst. It was found that **155b** maintained the biphasic property of ionic liquids and could be easily recovered by precipitation with diethyl ether. The catalyst could be recycled and reused at least six times with only slightly decreased activity.



Scheme 42

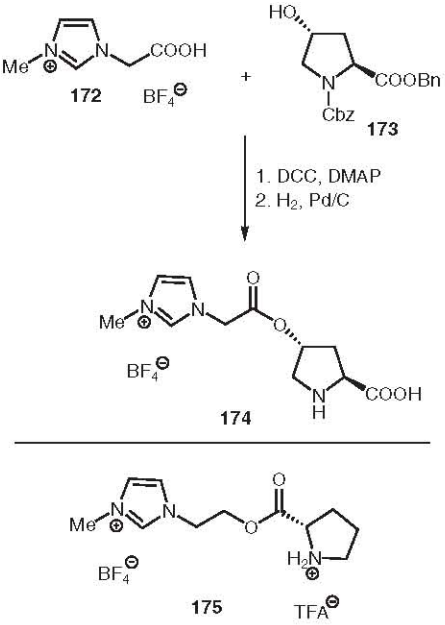
Very recently, Liang and co-workers[103] synthesized ionic-liquid-supported triazolyl pyrrolidine **171**; using (4-bromophenyl)methanol as starting material, compound **167** was synthesized via a Sonogashira coupling reaction and decomposition with potassium hydroxide. Treatment of **167** with thionyl chloride in pyridine gave **168**, and this reacted with 1-methylimidazole to give the quaternary salt **169**. The desired compound **171** was provided smoothly via the 1,3-dipolar cycloaddition of **169** and **170**[104] and subsequent anion metathesis (Scheme 43).



Scheme 43

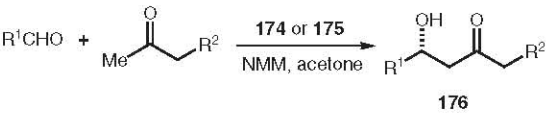
The catalytic activity of the ionic-liquid-supported organocatalyst **171** was evaluated in the Michael addition reaction of cyclohexanone to β-nitrostyrenes at room temperature; the expected adducts were obtained with good yields (up to 97%) and high selectivities (*syn*/*anti* = 97:3, 97% ee).

Miao and Chan reported the synthesis of the ionic-liquid-supported proline **174**[105] according to Scheme 44. Coupling of the ionic liquid support **172**[106,107] with **173** under *N*,*N*′-dicyclohexylcarbodiimide/4-(*N*,*N*-dimethylamino)pyridine conditions and hydrogenolysis afforded **174**. The ionic-liquid-supported proline trifluoroacetate salt **175** was prepared in a similar way, but including deprotection of the precursor with trifluoroacetic acid.



Scheme 44

The catalytic activities of **174** and **175** were examined in the direct asymmetric aldol reactions of 4-cyanobenzaldehyde carried out with one equivalent of *N*-methylmorpholine in acetone (Scheme 45). With **175** as catalyst, the aldol product **176** (R^1 = 4-CNC_6H_4, R^2 = H) was obtained with only 10% yield and 11% ee.



Scheme 45

The result was rather poor compared to that obtained with the unsupported L-proline, which gave 49% yield and 56% ee under identical conditions. When **174** was applied as the catalyst to the direct asymmetric aldol reaction in acetone under the same conditions, **176** was obtained in much better isolated yield (59%) and enantioselectivity (72% ee).

Lombardo et al.[108] reported onium-tagged prolines such as imidazolium-substituted proline bistriflimide **177** and butyldimethylammonium-substituted proline bistriflimide **178** (Figure 7). They were synthesized from 4-hydroxy-L-proline and their catalytic activity was tested in the direct asymmetric aldol condensation. For the reaction of acetone with various aldehydes, using 5 mol% of the catalyst, the yields of aldols varied from 50% to 85%, while the

enantioselectivities were in the 80–85% ee range. The catalytic protocol made use of a sixfold-lower amount of catalyst with respect to the preceding reports,[105,109–111] and afforded greater chemical yields and higher enantioselectivity.

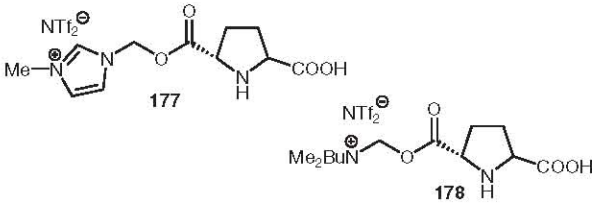


Figure 7

A new class of functionalized chiral ionic liquid phosphorous monodentate and diamidophosphites, **179–181** (Figure 8), were synthesized for the first time and applied as ligands in asymmetric transition-metal catalysis.[112] Up to 96% ee was achieved in the rhodium-catalyzed asymmetric hydrogenation of functionalized olefins, and up to 99% ee in the palladium-catalyzed allylic allylation.

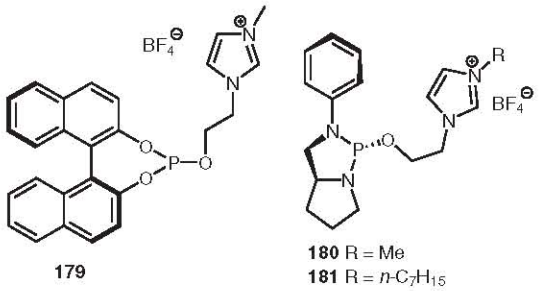


Figure 8

Imidazolium-tagged bis(oxazolines) **182** and **183** (Figure 9) were prepared and used as chiral ligands in the copper(II)-catalyzed Diels–Alder reaction of *N*-acryloyl- and *N*-crotonoyloxazolidines with cyclopentadiene in the ionic liquid 1-ethyl-3-methylimidazolium bis[(trifluoromethyl)sulfonyl]imide, [emim][NTf_2].[113] Complete conversion and enantioselectivities up to 95% were obtained within two minutes. In dichloromethane, one hour was required to reach completion, and only 16% ee was observed. The imidazolium-tagged catalysts were recycled ten times without any loss in activity or enantioselectivity, and showed much higher affinity for the ionic liquid phase during the recycling procedure than did the analogous anchored ligands.

Feng et al.[114] synthesized imidazolium-bearing Josiphos ligands starting from commercial Ugi amine. The two Josiphos ligands, **184** and **185**, were applied to the rhodium-catalyzed enantioselective hydrogenation of methyl acetamidoacrylate (**186**; R^1 = NHCOMe) and dimethyl itaconate (**186**; R^1 = CH_2COOMe) in biphasic cosolvent/ionic liquid combinations and were found to lead to 100% conversion and high efficiency (up to 99% ee) (Scheme 46).

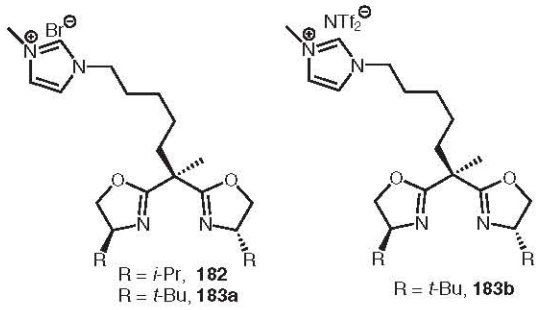
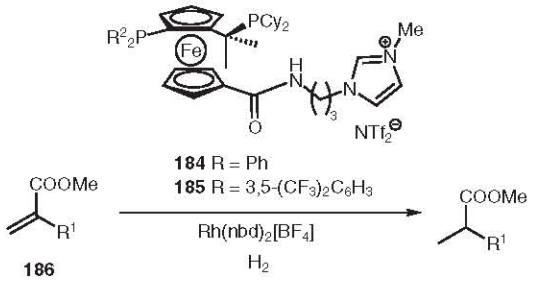


Figure 9



Scheme 46

4 Conclusion

The number of enantiopure ionic liquids that have been successfully applied as asymmetric catalytic reaction media is still very limited, but has developed substantially over the last two years. Liquids with chiral anions seem especially promising in this regard. Furthermore, the use of functionalized chiral ionic liquids in asymmetric catalysis has made efficient catalyst recovery possible.

Acknowledgment

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Preparation of aminals in water

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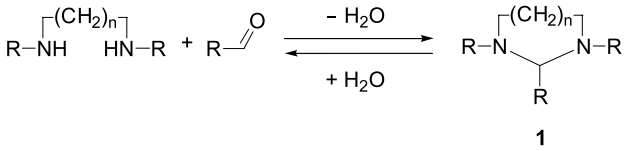
Abstract—Aminals, which are used as protecting groups in syntheses and are part of many biologically active compounds, are normally prepared from aldehydes and diamines under conditions that remove water in order to shift the equilibrium to the side of the aminal. Here we report for the first time that aminals can be prepared and isolated in pure water without a catalyst in high yield and purity.

1. Introduction

Aminals,[1] which are also known under the term *N*,*N*-acetals, are the aminated equivalents of acetals. The aminals can be either open chained or cyclic like aminal analogue **1**. Cyclic aminals can be used in synthesis as protecting groups for aldehydes.[2–6] In addition, five-membered ring aminals (imidazolidines) are important parts of biologically active compounds, for example, folic acid derivates.[7–9] Six-membered ring aminals (hexahydro-pyrimidines) are also often incorporated in biologically active molecules.[10,11]

Classical methods of preparing aminals involve the use of various drying agents, for example, potassium carbonate,[12] calcium sulfate,[13] boric anhydride[14] or removal of water by azeotropic distillation with benzene[15] in order to shift the equilibrium to the product side as shown in Scheme 1. If the aminals are crystallizing easily, reactions are performed in methanol or ethanol in the presence of a small amount of acetic acid.[2] If formaldehyde is used in the reaction, often an ethanol–water mixture is used as the solvent.[16]



1

Scheme 1.

We noticed from the literature that imines can be conveniently prepared in pure water without the presence of a catalyst from corresponding amines and aldehydes.[17] Since we were interested in preparing imidazolidines in a fast and easy way, we wanted therefore to investigate, if it would be also possible to prepare aminals in a similar way. So far aminals have never been synthesized and isolated in pure water. There is only one example known in the literature where the equilibrium constants for the formation of a few imidazolidines were measured in water via UV absorbance, however, no products were isolated.[18] In addition an aminal was prepared in a biphasic system of water and dichloromethane from diamines and glyoxal.[19]

The preparation of aminals in water is desirable, since reaction procedures, where water is used as a solvent instead of an organic solvent have become in recent years more and more important due to environmental consideration.[20,21]

2. Results and discussion

In order to follow the procedure of Simion et al. for the preparation of imines in water,[17] *N*,*N*′-dibenzyl-ethane-1,2-diamine (**2**) was strongly stirred in water and benzaldehyde was added to the emulsion. During 3 h of stirring a white precipitate formed which was filtered of and washed with water. After drying under vacuum the desired product **3a** was obtained in 91% yield (Table 1, entry 1) in high purity according to NMR spectral data and CHN-analysis. In comparison, when **2** was refluxed with benzaldehyde and a catalytic amount of *p*-toluene sulfonic acid in benzene on a Dean–Stark apparatus, the reaction took 16 h and a flash column chromatography with deactivated silica gel had to be performed to get **3a** in proper purity. When the reaction was carried out in abs. ethanol the product had to be purified again via flash column chromatography or via recrystallisation, which gave the product in only 62% yield. Finally, benzaldehyde was added to neat diamine **2** and a strong exothermic reaction was observed, which was completed

Keywords: Aminals; Water; Solvent; Imidazolidines; Protecting group.
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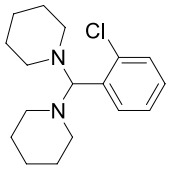
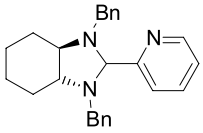
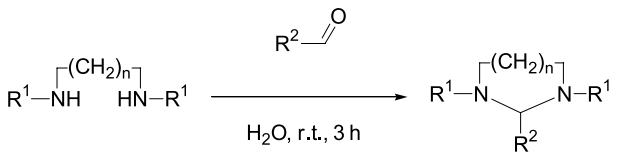
Table 1. Preparation of aminals

Entry		Diamine	Aldehyde		Aminal	Yield (%)
1	**2**	R^1=Bn, n=2	Benzaldehyde	**3a**	R^2=C_6H_5	91
2	**2**		2-Chlorobenzaldehyde	**3b**	R^2=1-(2-Cl–C_6H_4)	96
3	**2**		Pyridine-2-carbaldehyde	**3c**	R^2=2-(C_5H_4N)	99
4	**2**		Thiophene-2-carbaldehyde	**3d**	R^2=2-(C_4SH_3S)	99
5	**2**		2-Methoxybenzaldehyde	**3e**	R^2=1-(2-MeO–C_6H_4)	94
6[a]	**2**		2,4-Dichlorobenzaldehyde	**3f**	R^2=1-(2,4–Cl_2-C_6H_3)	96
7	**2**		Pentafluorobenzaldehyde	**3g**	R^2=1-(C_6F_5)	92
8[a]	**2**		4-Chlorobenzaldehyde	**3h**	R^2=1-(4-Cl–C_6H_4)	91
9[a]	**2**		2,6-Dichlorobenzaldhyde	**3i**	R^2=1-(2,6-Cl_2–C_6H_3)	88
10[b]	**2**		Propionaldehyde	**3j**	R^2=CH_2CH_3	85
11	**4**	R^1=Bn, n=3	Benzaldehyde	**5a**	R^2=C_6H_5	96
12	**4**		2-Chlorbenzaldehyde	**5b**	R^2=1-(2-Cl–C_6H_4)	88
13	**4**		Pyridine-2-carbaldehyde	**5c**	R^2=2-(C_5H_4N)	93
14	**6**	R^1=Bn, n=4	2-Chlorobenzaldehyde	**7a**	R^2=1-(2-Cl–C_6H_4)	99
15[b]	**8**	R^1=(*R*)-MeCHPh	2-Chlorobenzaldehyde	**9a**	R^2=1-(2-Cl–C_6H_4)	81
16[a,b]	**8**		4-Chlorobenzaldehyde	**9b**	R^2=1-(4-Cl–C_6H_4)	80
17[a]	**10**	R^1=Ph, n=2	2-Chlorobenzaldehyde	**11a**	R^2=1-(2-Cl–C_6H_4)	98
18[a]	**10**		Acetaldehyde	**11b**	R^2=CH_3	42
19	**12**	R^1=Me, n=2	Benzaldehyde	**13**	R^2=C_6H_5	67
20[c]	**14**	Piperidine	2-Chlorobenzaldehyde	**15**		99
21	**16**	(±)-*N*,*N*′-Dibenzyl-1,2-cyclohexanediamine	Pyridine-2-carbaldehyde	**17**		95

[a] Reaction temperature 80 °C.
[b] Reaction time 16 h.
[c] 2 equiv. piperidine.

after 15 min. However, due to the high temperature during the reaction many impurities next to **3a** were detected in the NMR spectra and again a flash column chromatography had to be carried out which gave the aminal **3a** in 60% yield. Given those results we concluded that for the preparation of aminal analogues of **3a** a reaction of diamines and benzaldehydes in water would be the most convenient and efficient procedure. The results are summarized in Table 1 Scheme 2.



Scheme 2.

First diamine **2** was reacted with different benzaldehydes to give the corresponding imidazolidines (entries 1–9). In all cases the obtained yields were very high (between 91 and 99%) and the products were pure according to NMR spectra and CHN-analysis. Electron deficient (entries 1–3, 6–9) and electron rich (entries 4, 5) benzaldehydes gave similar results. Even the hindered 2,6-dichloro-benzaldehyde gave the corresponding aminal **3i** in a good yield of 88% (entry 9). In cases where the melting points of the benzaldehydes where higher than room temperature, the mixtures were heated to 80 °C in order to melt the aldehydes and ensure the formation of an emulsion containing both reactants (entries 6, 8, 9, 16). When the benzaldehydes were not melted, yields where significantly lower.

In case of the polyfluorinated aminal **3g** (entry 7) the reaction was carried out in deoxygenated water under a nitrogen atmosphere. This was necessary to prevent the rapid oxidation of the aldehyde to the corresponding carboxylic acid before the formation of the desired aminal **3g** was finished. The product **3g** was isolated in a good yield of 92%. Since **3g** was a liquid, it was extracted from the reaction mixture with chloroform. To compare again methods, an attempt to prepare **3g** in benzene with a Dean–Stark apparatus under reflux was carried out, which gave no product at all. The same result was observed when abs. ethanol was chosen as a solvent for the reaction. When pentafluorobenzaldehyde was added to neat diamine **2** a strong exothermic reaction was observed, however no product was isolated, which may be due to the possible instability of either pentafluorobenzaldehyde or aminal **3g** at higher temperatures.

Aliphatic aldehydes can be applied in the described procedure also. Propionaldehyde gave with diamine **2** the expected aminal **3j** in 85% yield (entry 10). However, due to the lower reactivity of aliphatic aldehydes the reaction time had to be prolonged to 16 h. The scope of the reaction was extended with *N*,*N*′-dibenzyl-propane-1,3-diamine (**4**)[17,22] and *N*,*N*′-dibenzyl-butane-1,3-diamine (**6**)[22] which gave

with aldehydes cyclic aminals with a six- or a seven-membered ring in good yields between 88 and 99% (entries 11–14).

Furthermore *N*,*N*′-bis-((*R*)1-phenyl-ethyl)-ethane-1,2-diamine (**8**)[23] was used in the reaction with 2- and 4-chlorobenzaldehydes in order to have a more hindered system next to the nitrogen atoms. The reactions were complete after 16 h and the liquid products were isolated via extraction with chloroform giving the aminals **9a** and **9b** in 81 and 80% yield, respectively (entries 14, 15).

In addition *N*,*N*′-diphenyl-ethane-1,2-diamine (**10**) was forming with 2-chlorobenzaldehyde and acetaldehyde the aminals **11a** and **11b** in 98 and 42% yield, respectively (entries 17, 18). Since the melting point of the diamine **10** is 70 °C the reaction mixture was heated to 80 °C to melt the diamine. Aminal **13** was obtained in 67% yield from *N*,*N*′-dimethyl-ethane-1,2-diamine (**12**) and benzaldehyde (entry 19). Open aminals are also accessible as shown in entry 20, where 2 equiv. of piperidine (**14**) gave with 2-chlorobenzaldehyde the expected product in 99% yield (entry 20). Finally, the (±)-*trans*-cyclohexanediamine analogue **16** furnished with pyridine-2-carbaldehyde the aminal **17** in 95% yield (entry 21).

3. Conclusion

We were able to demonstrate a simple method to prepare cyclic aminals with various ring sizes in high yield and high purity in pure water without the presence of a catalyst. In addition it was possible to get access to aminals which could not be prepared via several different standard procedures.

4. Experimental

4.1. General experimental

N,*N*′-Dibenzyl-ethane-1,2-diamine (**2**), *N*,*N*′-diphenyl-ethane-1,2-diamine (**10**), *N*,*N*′-dimethyl-ethane-1,2-diamine (**12**), piperidine (**14**) and aldehydes were obtained from Aldrich and used without further purification. *N*,*N*′-Dibenzyl-propane-1,3-diamine (**4**),[17,22] *N*,*N*′-dibenzyl-butane-1,3-diamine (**6**),[22] *N*,*N*′-bis-((*R*)1-phenyl-ethyl)-ethane-1,2-diamine (**8**)[23] and (±)-*N*,*N*′-dibenzyl-1,2-cyclohexanediamine (**16**)[24] were prepared according to literature procedures. The reactions were carried out in dest. water.

Flash column chromatography[25] was performed on Sorbisil C-60. All reactions were monitored by TLC with Merck Silica gel 60 F_{254} plates. Elemental analyses were carried out by the Microanalytical Laboratory of the Institut für Pharmazeutische Chemie der Universität Braunschweig. Infrared spectra were recorded on a Perkin–Elmer 2000 FT-IR System FTIR instrument. NMR spectra were performed in $CDCl_3$ at ambient temperature on a Bruker AMX 400 and a Bruker AC 200F. Mass spectra were recorded on Hewlett–Packard 5898B (at 70 eV). Melting points were taken with an apparatus after Dr Tottoli and are uncorrected.

4.2. Preparation of aminals

General procedure. A diamine (1.00 mmol) was added to water (1.5 mL) and an aldehyde (1.00 mmol) was added. The mixture was vigorously stirred for 3 h at rt. For exceptions in temperature and reaction times see Table 1. The precipitate was isolated by filtration, washed with water (5 mL) and dried under vacuum to afford the desired product. In case the product was a liquid, the reaction mixture was extracted with $CHCl_3$ (3×5 mL) and the combined organic phases were dried (Na_2SO_4) and the solvent evaporated.

4.2.1. 1,3-Dibenzyl-2-phenyl-imidazolidine (3a). As a white solid (91%). Mp 97–98 °C (Lit.[26] 99 mp °C); MS (EI), *m*/*e* 328 (M^+, 25%), 327 (M^+-H, 25), 251 (M^+-Ph, 100), 91 (80); IR (KBr) 2780s, 1490s, 1450s, 1161s, 700s cm^{-1}; ^1H NMR (200 MHz) δ 7.67–7.16 (m, 15H), 3.84 (s, 1H), 3.79 (d, *J*=13.0 Hz, 2H), 3.22–3.13 (m, 2H), 3.20 (d, *J*=13.2 Hz, 2H), 2.53–2.45 (m, 2H); ^{13}C NMR (50 MHz) δ 140.3, 139.2, 129.5, 128.6, 128.2, 128.1, 126.8, 89.0, 56.9, 50.6. Anal. Calcd for $C_{23}H_{24}N_2$: C, 84.11; H, 7.36; N, 8.53, found: C, 83.80; H, 7.37; N, 8.48. The spectral data were consistent with literature values.[27,28]

4.2.2. 1,3-Dibenzyl-2-(2-chloro-phenyl)-imidazolidine (3b). As a white solid (96%). Mp 96 °C (Lit.[29] 96–97 °C); MS (EI), *m*/*e* 361 (M^++H, 25%), 251 (100), 91 (75); IR (KBr) 2793m, 1365m, 1151s, 757vs, 698vs cm^{-1}; ^1H NMR (400 MHz) δ 8.14 (d, *J*=7.8 Hz, 1H), 7.45–7.25 (m, 13H), 4.70 (s, 1H), 3.85 (d, *J*=13.2 Hz, 2H), 3.41 (d, *J*=13.2 Hz, 2H), 3.26–3.23 (m, 2H), 2.64–2.61 (m, 2H); ^{13}C NMR (100 MHz) δ 139.7, 138.2, 136.0, 131.8, 129.8, 129.3, 128.9, 128.6, 127.7, 127.3, 83.6, 57.3, 51.2. Anal. Calcd for $C_{23}H_{23}ClN_2$: C, 76.12; H, 6.39; N, 7.72, found: C, 75.82; H, 6.32; N, 7.55.

4.2.3. 2-(1,3-Dibenzyl-imidazolidin-2-yl)-pyridine (3c). As a white solid (99%). Mp 80–81 °C; MS (EI), *m*/*e* 329 (M^++H, 5%), 251 (100), 197 (10), 238 (10), 91 (80), 65 (10); IR (KBr) 2792m, 1493m, 1434s, 1360m, 1135m, 1148m, 781s, 749s, 696vs cm^{-1}; ^1H NMR (400 MHz) δ 8.56–8.55 (m, 1H), 8.01 (dt, *J*=8.0, 1.0 Hz, 1H), 7.79 (td, *J*=7.7, 1.8 Hz, 1H), 7.30–7.20 (m, 11H), 4.14 (s, 1H), 3.86 (d, *J*=13.4 Hz, 2H), 3.41 (d, *J*=13.4 Hz, 2H), 3.27–3.23 (m, 2H), 2.61–2.57 (m, 2H); ^{13}C NMR (100 MHz) δ 161.8, 148.6, 139.4, 137.3, 128.9, 128.5, 127.2, 123.7, 123.5, 89.9, 57.4, 51.3. Anal. Calcd for $C_{22}H_{23}N_3$: C, 80.21; H, 7.04; N, 12.76, found: C, 79.89; H, 7.12; N, 12.88.

4.2.4. 1,3-Dibenzyl-2-thiophen-2-yl-imidazolidine (3d). As a white solid (99%). Mp 122 °C; MS (EI), *m*/*e* 333 (M^++H, 1%), 124 (50), 97 (30), 91 (100); IR (KBr) 1307s, 1161s, 744s, 717s, 698s cm^{-1}; ^1H NMR (400 MHz) δ 7.42–6.99 (m, 13H), 4.82 (s, 1H), 3.96 (d, *J*=12.9 Hz, 2H), 3.29 (d, *J*=12.9 Hz, 2H), 3.20–3.17 (m, 2H), 2.56–2.52 (m, 2H); ^{13}C NMR (100 MHz) δ 146.4, 139.4, 129.0, 128.6, 128.0, 127.3, 127.1, 126.2, 84.0, 57.3, 50.7. Anal. Calcd for $C_{21}H_{22}N_2S$: C, 75.41; H, 6.63; N, 8.38, found: C, 75.41; H, 6.61; N, 8.77.

4.2.5. 1,3-Dibenzyl-2-(2-methoxy-phenyl)-imidazolidine (3e). As a white solid (94%). Mp 70 °C; MS (EI), *m*/*e* 357

(M^++H, 20%), 251 (100), 148 (15), 121 (20), 91 (100), 65 (20); IR (KBr) 2795s, 2492s, 1380s, 1239s, 1153s, 752s, 698s cm^{-1}; ^1H NMR (400 MHz) δ 8.00 (dd, J=7.6, 1.4 Hz, 1H), 7.32–7.03 (m, 12H), 6.87 (d, J=8.3 Hz, 1H), 3.59 (s, 1H), 3.84 (s, 3H), 3.80 (d, J=13.2 Hz, 2H), 3.29 (d, J=13.2 Hz, 2H), 3.17–3.14 (m, 2H), 2.56–2.52 (m, 2H); ^{13}C NMR (100 MHz) δ 159.5, 140.0, 130.3, 129.5, 128.4, 121.5, 110.6, 80.1, 55.9, 51.1. Anal. Calcd for $C_{24}H_{26}N_2O$: C, 80.41; H, 7.31; N, 7.81, found: C, 80.3; H, 7.43; N, 7.71.

4.2.6. 1,3-Dibenzyl-2-(2,4-dichloro-phenyl)-imidazolidine (3f). As a yellow solid (96%). Mp 84 °C; MS (EI), *m/e* 395 (M^++H, 15%), 251 (100), 91 (80); IR (KBr) 2804s, 1337s, 1152s, 854s, 697vs cm^{-1}; ^1H NMR (400 MHz) δ 8.03 (d, J=8.3 Hz, 1H), 7.39–7.35 (m, 2H), 7.31–7.20 (m, 10H), 4.60 (s, 1H), 3.78 (d, J=13.1 Hz, 2H), 3.38 (d, J=13.1 Hz, 2H), 3.25–3.15 (m, 2H), 2.65–2.55 (m, 2H); ^{13}C NMR (100 MHz) δ 139.4, 137.2, 136.4, 134.7, 132.8, 128.9, 128.8, 128.6, 128.1, 127.3, 83.1, 57.2, 51.2. Anal. Calcd for $C_{23}H_{22}Cl_2N_2$: C, 69.52; H, 5.58; N, 7.05, found: C, 69.33; H, 5.46; N, 6.81.

4.2.7. 1,3-Dibenzyl-2-pentafluorophenyl-imidazolidine (3g). Reaction was carried out in deoxygenated water under a nitrogen atmosphere. The crude oily product was purified by flash chromatography (FCC) (eluant: 2.5% ethyl acetate −0.5% triethylamine–hexane) through a short pad of silica to afford the *title compound* **3g** as a clear oil (92%). MS (EI), *m/e* 418 (M^+, 10%), 251 (40), 91 (100); IR (KBr) 2795s, 1500s, 954s, 740s, 700s cm^{-1}; ^1H NMR (400 MHz) δ 7.22–7.18 (m, 10H), 4.61 (s, 1H), 3.75 (d, J=13.3 Hz, 2H), 3.66 (d, J=13.2 Hz, 2H), 3.32–3.29 (m, 2H), 2.72–2.69 (m, 2H); ^{13}C NMR (100 MHz) δ 138.8, 128.7, 128.5, 127.5, 79.8, 58.3, 52.0. Anal. Calcd for $C_{23}H_{19}N_2F_5$: C, 66.02; H, 4.58; N, 6.70, found: C, 65.67; H, 4.56; N, 6.55.

4.2.8. 1,3-Dibenzyl-2-(4-chloro-phenyl)-imidazolidine (3h). As a white solid (91%). Mp 106 °C (Lit.[29] 109 °C); MS (EI), *m/e* 361 (M^++H, 25%), 251 (75), 152 (20), 125 (20), 91 (100), 65 (20); IR (KBr) 2804m, 1493m, 1148m, 1186m, 822s, 698vs cm^{-1}; ^1H NMR (400 MHz) δ 7.64–7.61 (m, 2H), 7.44–7.38 (m, 2H), 7.33–7.22 (m, 10H), 4.01 (s, 1H), 3.79 (d, J=13.2 Hz, 2H), 3.28–3.20 (m, 4H), 2.57–2.53 (m, 2H); ^{13}C NMR (100 MHz) δ 139.6, 139.4, 134.6, 131.2, 128.9, 128.8, 128.6, 127.3, 88.6, 57.3, 51.1. Anal. Calcd for $C_{23}H_{23}ClN_2$: C, 76.12; H, 6.39; N, 7.72, found: C, 76.00; H, 6.39; N, 7.65.

4.2.9. 1,3-Dibenzyl-2-(2,6-dichloro-phenyl)-imidazolidine (3i). As a white solid (88%). Mp 145 °C; MS (EI), *m/e* 495 (M^++H, 5%), 251 (90), 91 (100); IR (KBr) 2792m, 1492m, 1436s, 1377m, 1337m, 1148m, 782m, 766m, 737vs, 698s cm^{-1}; ^1H NMR (400 MHz) δ 7.37–7.11 (m, 13H), 5.07 (s, 1H), 3.87 (d, J=13.6 Hz, 2H), 3.58 (d, J=13.6 Hz, 2H), 3.36–3.33 (m, 2H), 2.62–2.58 (m, 2H); ^{13}C NMR (100 MHz) δ 140.1, 137.7, 135.2, 129.5, 128.6, 128.5, 128.2, 127.1, 85.0, 58.2, 51.8. Anal. Calcd for $C_{23}H_{22}Cl_2N_2$: C, 69.52; H, 5.58; N, 7.06, found: C, 69.47; H, 5.59; N, 6.88.

4.2.10. 1,3-Dibenzyl-2-ethyl-imidazolidine (3j). The crude oil was purified by flash chromatography (FCC) (eluant: 2.5% ethyl acetate −0.5% triethylamine–hexane) to afford the title compound **3j** as a clear oil. (85%). MS (EI), *m/e* 280 (M^+, 5%), 251 (M^+−Et, 100); IR (neat) 2925s, 2785s, 1495s, 1455s, 1345s, 1028s, 700s cm^{-1}; ^1H NMR (200 MHz) δ 7.29–7.19 (m, 10H), 3.98 (d, J=13.1 Hz, 2H), 3.38 (d, J=13.3 Hz, 2H), 3.14 (t, J=3.8 Hz, 1H), 2.99–2.86 (m, 2H), 2.47–2.38 (m, 2H), 1.73–1.60 (m, 2H), 1.11–0.92 (m, 3H); ^{13}C NMR (50 MHz) δ 139.8, 128.6, 128.2, 126.8, 85.6, 58.5, 50.6, 24.4, 8.16. The spectral data were consistent with literature values.[27,28]

4.2.11. 1,3-Dibenzyl-2-phenyl-hexahydro-pyrimidine (5a). As a white solid (96%). Mp 113–114 °C (Lit.[30] 120 °C); MS (EI), *m/e* 341 (M^+−H, 10%), 265 (M^+−Ph, 100), 91 (95); IR (KBr) 2950s, 2795s, 1490s, 1450s, 1095s, 700s cm^{-1}; ^1H NMR (200 MHz) δ 7.69–7.13 (m, 15H), 3.612 (d, J=13.2 Hz, 2H), 3.608 (s, 1H), 3.02–2.95 (m, 2H), 2.85 (d, J=13.1 Hz, 2H), 2.11–1.41 (m, 4H); ^{13}C NMR (50 MHz) δ 141.9, 139.7, 129.6, 128.6, 128.3, 128.2, 128.0, 126.6, 89.0, 58.4, 51.8, 24.4. Anal. Calcd for $C_{24}H_{26}N_2$: C, 84.17; H, 7.65; N, 8.18, found: C, 84.20; H, 7.65; N, 8.13.

4.2.12. 1,3-Dibenzyl-2-(2-chloro-phenyl)-hexahydro-pyrimidine (5b). As a white solid (88%). Mp 94–96 °C; MS (EI), *m/e* 375 (M^++H, 5%), 365 (100), 91 (80); IR (KBr) 2923s, 1367s, 1098s, 756vs, 739vs, 698vs cm^{-1}; ^1H NMR (400 MHz) δ 8.19–8.16 (m, 1H), 7.41–7.19 (m, 13H), 4.34 (s, 1H), 3.58 (d, J=13.2 Hz, 2H,), 3.03–2.99 (m, 4H), 2.15–2.08 (m, 2H), 1.92–1.83 (m, 1H), 1.51–1.47 (m, 1H); ^{13}C NMR (100 MHz) δ 139.9, 136.1, 131.3, 129.5, 128.9, 128.7, 128.5, 128.0, 127.7, 127.1, 83.2, 58.1, 51.3, 25.1. Anal. Calcd for $C_{24}H_{25}ClN_2$: C, 76.48; H, 6.69; N, 7.43, found: C, 76.08; H, 6.69; N, 7.36.

4.2.13. 1,3-Dibenzyl-2-pyridin-2-yl-hexahydro-pyrimidine (5c). As a white solid (93%). Mp 80–81 °C; MS (EI), *m/e* 344 (M^++H, 25%), 265 (M^+−pyridinyl, 100), 91 (80); IR (KBr) 3060s, 2930s, 2790s, 1590s, 1490s, 1450s, 1440s, 1170s, 980s, 820s, 790s cm^{-1}; ^1H NMR (400 MHz) δ 8.58–8.56 (m, 1H), 8.07–8.04 (m, 1H), 7.77 (td, J=7.6, 1.7 Hz, 1H), 7.28–7.21 (m, 11H), 3.90 (s, 1H), 3.50 (d, J=13.6 Hz, 2H), 3.06 (d, J=13.6 Hz, 2H), 3.05–3.01 (m, 2H), 2.13 (td, J=11.8, 2.8 Hz, 2H), 1.94–1.85 (m, 1H), 1.56–1.52 (m, 1H); ^{13}C NMR (100 MHz) δ 163.1, 148.4, 139.7, 137.5, 129.0, 128.5, 127.1, 124.0, 123.6, 89.5, 58.7, 51.8, 25.0. Anal. Calcd for $C_{23}H_{25}N_3$: C, 80.43; H, 7.34; N, 12.23, found: C, 80.03; H, 7.28; N, 12.17.

4.2.14. 1,3-Dibenzyl-2-(2-chloro-phenyl)-[1,3]diazepane (7a). As a white solid (98%). Mp 67 °C; MS (EI), *m/e* 390 (M^++H, 1%), 160 (80), 91 (100); IR (KBr) 2791m, 1085s, 1070s, 762vs, 751vs, 697vs cm^{-1}; ^1H NMR (400 MHz) δ 8.10 (d, J=4 Hz, 1H), 7.45–7.19 (m, 13H), 5.04 (s, 1H), 3.90–3.84 (m, 2H) 3.70–3.66 (m, 2H) 3.02–2.97 (m, 2H), 2.88–2.82 (m, 2H), 1.71–1.55 (m, 4H); ^{13}C NMR (100 MHz) δ 140.6, 140.4, 135.6, 130.2, 129.2, 128.6, 128.6, 128.5, 127.0, 126.8, 82.6, 55.5, 48.9, 26.2. Anal. Calcd for $C_{22}H_{23}N_3$: C, 76.80; H, 6.96; N, 7.17, found: C, 76.42; H, 7.05; N, 6.99.

4.2.15. 2-Chlorophenyl-1,3-bis-((*R*)-1-phenyl-ethyl)-imidazoline (9a). The crude product was purified by Kugelrohr distillation (0.5 mbar, 200 °C) to afford the title compound **9a** as a clear yellow oil (81%). $[\alpha]_D^{25}$=−30 (c=1 in $CHCl_3$),

MS (EI), *m/e* 391 (M^++H, 15%), 279 (M^+−PhCl, 100), 105 (65); IR (neat) 2970s, 1490s, 1450s, 1370s, 1030s, 760s, 700s cm^{-1}; ^1H NMR (400 MHz) δ 7.98 (d, J=8.0 Hz, 1H), 7.38–7.14 (m, 13H), 4.97 (s, 1H), 3.81–3.71 (m, 2H), 3.20–3.14 (m, 1H), 2.90–2.85 (m, 1H), 2.74–2.63 (m, 2H), 1.42 (d, J=6.5 Hz, 3H), 1.15 (d, J=6.5 Hz, 3H); ^{13}C NMR (100 MHz) δ 145.0, 144.4, 141.9, 134.6, 132.3, 129.2, 128.9, 128.6, 128.2, 127.9, 127.7, 127.2, 127.1, 126.8, 78.5, 62.2, 55.4, 50.0, 49.1, 44.7, 23.4, 14.4. Anal. Calcd for $C_{25}H_{27}N_2Cl$: C, 76.81; H, 6.97; N, 7.17, found: C, 76.43; H, 6.95; N, 7.12.

4.2.16. 4-Chlorophenyl-1,3-bis-((*R*)-1-phenyl-ethyl)-imidazoline (9b). The crude product was purified by Kugelrohr distillation (0.5 T, 200 °C) to afford the title compound **9b** as a clear yellow oil (80%). $[\alpha]_D^{25}$=−70 (c=1 in $CHCl_3$), MS (EI), *m/e* 391 (M^++H, 25%), 279 (M^+−PhCl, 100), 105 (65); IR (neat) 2970s, 1490s, 1450s, 1090s, 700s cm^{-1}; ^1H NMR (400 MHz) δ 7.26–7.13 (m, 14H), 4.35 (s, 1H), 3.66 (q, J=6.5 Hz, 1H), 3.56 (q, J=6.5 Hz, 1H), 3.14–3.02 (m, 2H), 2.90–2.82 (m, 2H), 1.33 (d, J=6.5 Hz, 3H), 1.22 (d, J=6.5 Hz, 3H); ^{13}C NMR (100 MHz) δ 144.6, 144.3, 144.4, 133.1, 130.7, 128.5, 128.3, 128.09, 128.06, 127.99, 127.2, 127.1, 82.0, 60.3, 59.2, 48.3, 47.0, 23.7, 17.9. Anal. Calcd for $C_{25}H_{27}N_2Cl$: C, 76.81; H, 6.97; N, 7.17, found: C, 76.55; H, 7.02; N, 7.16.

4.2.17. 2-(2-Chloro-phenyl)-1,3-diphenyl-imidazolidine (11a). As a white solid (99%). Mp 128 °C (Lit.[31] 128–129 °C). The spectral data were consistent with literature values.[31]

4.2.18. Methyl-1,3-diphenyl-imidazolidine (11b). The crude product was filtered of and recrystallised from methanol to afford the title compound **11b** as a white solid. (42%). Mp 95–96 °C (Lit.[32] mp 97 °C). The spectral data were consistent with literature values.[33]

4.2.19. 1,3-Dimethyl-2-phenyl-imidazolidine (13). As a clear liquid (67%). The spectral data were consistent with literature values.[34]

4.2.20. 1,1′-(2-Chloro-phenylmethanediyl)-bis-piperidine (15). 2 equiv. piperidine were used in the reaction. The product was isolated as a yellow liquid (99%). (Lit.[35] 62 °C). MS (EI), *m/e* 292 (M^+, 5%), 208 (M^+, −piperidinyl, 95%), 125 (90), 84 (100); IR (neat) 2930s, 1470s, 1440s, 1270s, 1100s, 910s, 735s cm^{-1}; ^1H NMR (200 MHz) δ 7.44–7.12 (m, 4H), 4.39 (s, 1H), 2.84–2.28 (m, 8H), 1.56–1.34 (m, 12H); ^{13}C NMR (50 MHz) δ 134.8, 134.2, 130.0, 129.3, 127.7, 125.4, 83.1, 49.8, 26.2, 25.2.

4.2.21. (±)-1,3-Dibenzyl-2-(2-pyridinyl)-octahydrobenzoimidazole (17). As a white solid (95%). Mp 49–50 °C; MS (EI), *m/e* 383 (M^+, 5%), 305 (M^+, −pyridinyl, 50), 187 (25), 91 (100); IR (KBr) 2925s, 2800s, 1590s, 1450s, 1440s, 1145s, 700s cm^{-1}; ^1H NMR (400 MHz) δ 8.40–8.38 (m, 1H), 7.52 (td, J=7.6, 1.9 Hz, 1H), 7.38–7.35 (m, 1H), 7.20–7.05 (m, 11H), 4.74 (s, 1H), 3.84 (d, J=13.8 Hz, 1H), 3.79 (d, J=13.7 Hz, 1H), 3.53 (d, J=14.4 Hz, 1H), 3.47 (d, J=14.4 Hz, 1H), 2.99–2.94 (m, 1H), 2.55–2.49 (m, 1H), 1.83–1.70 (m, 2H), 1.31–1.13 (m, 2H); ^{13}C NMR (100 MHz) δ 162.0, 148.6, 141.3, 139.6, 135.8, 129.4, 128.4, 128.2, 128.1, 126.9, 126.7, 124.5, 122.5, 87.8, 69.3, 67.9, 56.9, 52.9, 30.6, 30.3, 25.0, 24.9. Anal. Calcd for $C_{26}H_{29}N_3$: C, 81.42; H, 7.62; N, 10.96, found: C, 81.22; H, 7.65; N, 10.90.

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ARTICLE

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Imidazolinium salts as catalysts for the aza-Diels–Alder reaction

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Various easily accessible imidazolinium salts have been found to be capable of catalysing an aza-Diels–Alder reaction with a range of imines and Danishefsky's diene, giving the desired products in good to excellent yields. The influence of the counter-anions on the reactivity has been explored. These salts could contribute to the field of metal-free catalysis/organocatalysis.

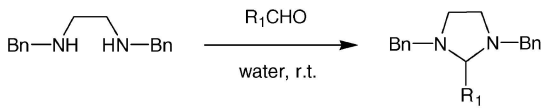
Introduction

Imidazolinium salts are important precursors for N–C–N carbene ligands, which have found widespread application in various metal-catalysed reactions.[1] However, these salts, which possess weak Lewis acidity in the imidazolinium unit, have been rarely used as catalysts. In fact, to the best of our knowledge, there has been only one report of an imidazolinium salt being used as a catalyst, in which the salt catalysed the opening of an epoxide.[2] Depending which mesomeric structure is used to describe imidazolinium cations, they can also be described as imidazolidinium[3] cation. In addition, they are also known as 4,5-dihydroimidazolium.

Since imidazolinium salts do not contain any metals, they could contribute to the field of organocatalysis,[4] which has attracted much interest in recent years. This research area is part of the larger field of homogeneous catalysis, that has so far been mainly dominated by metal–ligand systems.[5,6] In addition to covalent-based organocatalytic systems,[7–13] catalysts that activate carbonyl compounds *via* hydrogen bonds have been found.[14] In addition, metal-free Lewis bases,[15] Lewis acids[2,16–21] and Brønsted acids[22,23] have been used as catalysts. However, the number of examples of organocatalysts in the literature remains small, compared to metal-based systems.[4] This prompted us to present here our investigation of imidazolinium salts as metal-free Lewis acid catalysts for the aza-Diels–Alder reaction, which is an important method for the preparation of nitrogen-containing six-membered rings,[24] and has been catalysed by various catalytic systems, either achiral[25–35] or chiral.[36]

Results and discussion

Initially, various imidazolidines were prepared from secondary diamines and aldehydes in water following a literature procedure, as shown in Scheme 1.[37]



Scheme 1

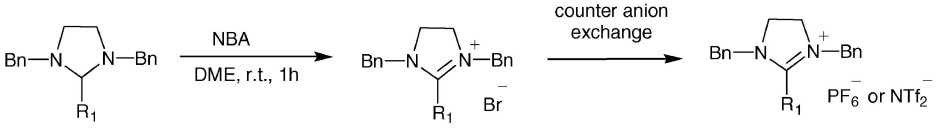
The imidazolidenes were then transformed into imidazolinium bromide salts by treating them with *N*-bromoacetamide (Scheme 2), using a modified literature procedure.[38] After stirring in DME for 1 h, the salts precipitated and were isolated by filtration. In cases where no precipitate was formed, diethyl ether was added in order to isolate the salts as solids or oils, which were washed with diethyl ether after decanting the solvent from the reaction mixture. The results are presented in Table 1. All salts have various aryl groups in the 2-position. Although the aryl groups in these salts are nearly perpendicular to the imidazolinium ring,[39] it may be still possible to slightly tune the positive charge of the imidazolinium unit through the σ-bond framework. All bromide salts were obtained in very good yields (88–99%). As well as substituted (runs 3, 6 and 9, Table 1) and polyfluorinated aryls (run 11, Table 1), the reaction also tolerated the electron-deficient heteroaromatic pyridinyl substituent (run 13, Table 1) and the electron-rich thiophenyl substituent (run 15, Table 1).

Table 1 Preparation of imidazolinium salts[a]

Run	Imidazolidines		Imidazolinium salts		Yield (%)[b]
		R_1		Anion	
1	**1**	C_6H_5	**2a**	Br	95
2	**1**	C_6H_5	**2b**	PF_6	86
3	**3**	1-(2-Cl–C_6H_4)	**4a**	Br	93
4	**3**	1-(2-Cl–C_6H_4)	**4b**	PF_6	95
5	**3**	1-(2-Cl–C_6H_4)	**4c**	NTf_2	71
6	**5**	1-(4-Cl–C_6H_4)	**6a**	Br	88
7	**5**	1-(4-Cl–C_6H_4)	**6a**	PF_6	89
8	**5**	1-(4-Cl–C_6H_4)	**6c**	NTf_2	90
9	**7**	1-(2,4-Cl_2–C_6H_3)	**8a**	Br	91
10	**7**	1-(2,4-Cl_2–C_6H_3)	**8b**	PF_6	90
11	**9**	C_6F_5	**10a**	Br	90
12	**9**	C_6F_5	**10b**	PF_6	90
13	**11**	2-(C_5H_4N)	**12a**	Br	99
14	**11**	2-(C_5H_4N)	**12b**	PF_6	71
15	**13**	2-(C_4H_3S)	**14a**	Br	90
16	**13**	2-(C_4H_3S)	**14b**	PF_6	92

[a] See Experimental for details. [b] Isolated yields.

All bromide salts were highly hygroscopic and difficult to handle, and therefore CHN-analyses were carried out after changing the bromide anion into a hexafluorophosphate and/or bis(trifluoromethylsulfonyl)imide anion. For the anion exchange the bromide salts were dissolved in DCM and stirred with 1.5 equiv. of either KPF_6 or $LiNTf_2$ (Scheme 2). The mixture was washed with water for 1 h. This was repeated two times. The



Scheme 2

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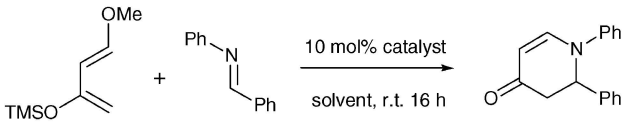
Table 2 Aza-Diels–Alder reactions with 10 mol% catalyst at r.t.[a]

Run	Catalyst	Solvent	Yield (%)[b]
1	—	MeCN	10
2	—	DCM	0
3	—	Toluene	0
4	**2a**	MeCN	14
5	**2b**	MeCN	46
6	**4b**	MeCN	63
7	**4c**	MeCN	98
8[c]	**4c**	Toluene	41
9[d]	**4c**	DCM	79
10	**6a**	MeCN	56
11	**6b**	MeCN	76
12	**6c**	MeCN	82
13	**8b**	MeCN	72
14	**10b**	MeCN	95
15	**10b**	DCM	40
16[e]	**10b**	MeCN	94
17[f]	**10b**	MeCN	76
18[g]	**10b**	MeCN	73
19	**12b**	MeCN	73
20	**12b**	DCM	24
21	**14b**	MeCN	47

[a] See Experimental for details. [b] Isolated yields. [c] Reaction time 48 h [d] Reaction time 6 days. [e] 5 mol% **10b**. [f] 2.5 mol% **10b**. [g] 1 mol% **10b**.

solvent was evaporated and the salts dried under high vacuum. The results are presented in Table 1. All PF_6 and NTf_2 salts were isolated in very good yields between 71 and 95% (runs 2, 4, 5, 7, 8, 10, 12, 14 and 16, Table 1). All salts gave a correct CHN-analysis, indicating that the corresponding bromide salts were also obtained in high purity. The hexafluorophosphate salt **6b** and the two bis(trifluoromethylsulfonyl)imides **4c** and **6c** have melting points of 71, 83 and 80 °C, respectively. Since their melting points are lower than 100 °C, these three salts belong by definition to the family of ionic liquids.[40,41]

The salts were tested as catalysts in the aza-Diels–Alder reaction of *N*-benzylideneaniline (**16**) and Danishefsky's diene (**15**). The reaction was performed for 16 h at room temperature in various solvents (Scheme 3, Table 2). First, control reactions were carried out in acetonitrile, DCM and toluene. The reaction with the last two solvents gave no product at all (runs 2 and 3, Table 2). In acetonitrile the expected product **17** was isolated in 10% yield (run 1, Table 2).



15 **16** **17**

Scheme 3

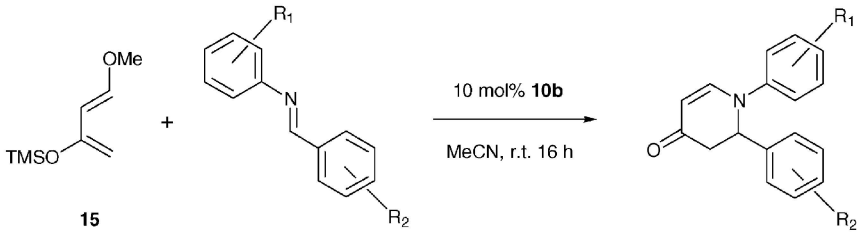
The first compound tested was the bromide salt **2a** bearing a phenyl group at the C-2 position, which led to a yield of 14%, using acetonitrile as the solvent (run 4, Table 2). By changing the counter-anion to PF_6, the yield increased to 46% (run 5, Table 2). This increase could be expected, since the PF_6 anion is a weaker coordinating anion[42,43] than the bromide, which explains the higher reactivity of salt **2b**. When the salt **4b** was tested, the yield increased to 63% (run 6, Table 2), which may be related to the more electron-withdrawing 2-chlorophenyl substituent of the salt. The catalyst **4c** gave the desired product in a yield of 98% (run 7, Table 2). This increase in yield can be attributed to the NTf_2 anion, which is even less coordinating than the PF_6 anion. Catalyst **4c** was then used in different solvents. In toluene a yield of 41% was found, however, the reaction time was extended to 48 h (run 8, Table 2), while in DCM a yield of 79% was obtained after 6 days (run 9, Table 2). The lower yields in these two solvents and the longer reaction times can be rationalised by their lower capability to dissociate salts compared to acetonitrile. Next, the salts **6a**, **6b** and **6c** with a 4-chlorophenyl substituent were tested. As expected, the yields increased from the bromide **6a** to the hexafluorophosphate **6b** to the bis(trifluoromethylsulfonyl)imide **6c**, giving 56, 76 and 82%, respectively (runs 10, 11 and 12, Table 2). The yields for the 4-chlorophenyl and 2-chlorophenyl substituents were quite similar. When salt **8b** with a 2,4-dichlorophenyl substituent was applied, the yield obtained was nearly the same as for **6b** (run 13, Table 2). Attention was then directed to the salt **10b**, which has a pentafluorophenyl substituent at the 2-position. The polyfluorinated substituent may have two positive effects: first, it can increase the positive charge of the imidazolinium unit, due to the strong electron-withdrawing capability of the fluorine atoms; second, the fluorine atoms are lipophilic and can help to increase the solubility of the salt. Under standard reaction conditions, salt **10b** gave a yield of 95% in acetonitrile (run 14, Table 2). When DCM was used as the solvent, the desired product was isolated in 40% yield (run 15, Table 2). In addition, three more reactions in acetonitrile were carried out with **10b**, using a catalyst loading of 5, 2.5 and 1 mol%, which gave the product in 94, 76 and 73% yield, respectively (runs 16, 17 and 18, Table 2). In acetonitrile, the salt **12b** gave a yield of 73% (run 19, Table 2), which is comparable with salts **4b**, **6b** and **8b** (runs 6, 11 and 13, Table 2). When **12b** was evaluated in DCM, a poor yield of 24% was obtained (run 20, Table 2), which is nearly half that obtained with the more lipophilic salt **10b** (run 15, Table 2). Finally, in acetonitrile, salt **14b** gave a moderate yield of 47% (run 21, Table 2). Clearly, the electron-rich thiophenyl substituent reduces the Lewis acidity of the imidazolinium cation.

With the standard conditions using 10 mol% of salt **10b**, various imines were tested in the aza-Diels–Alder reaction with Danishefsky's diene (**15**) (Scheme 4). The results are summarised in Table 3. It was possible to observe that neither an electron-withdrawing, nor an electron-donating substituent on the aryl ring of the nitrogen atom of the imine had an influence on the reaction. All three imines **16**, **18** and **20** gave similar good yields (runs 1, 2 and 3, Table 3). The scope of the reaction was then explored by using different aryls attached to the carbon atom of the imine. When an electron-withdrawing chlorine atom was placed in the *para*-position of the aryl, the yield dropped slightly to 72% (run 4, Table 3). When an electron-donating methoxy group was present at the *ortho* position, the yield decreased to 57% (run 5, Table 3), while at the *para*-position an even lower yield of 45% was found (run 7, Table 3). Finally, the imines **26** and **30** furnished the desired products in 50 and 93% yield, respectively (runs 6 and 8, Table 3). Interestingly, the 4-nitrophenyl group of imine **30** had a significance influence on the yield, while the 2-pyridinyl group of imine **26** did not, although both groups are electron-deficient.

At the end, the salt **10b** was tested as a catalyst in an aza-Diels–Alder reaction with imine **16** and 3,4-dihydro-2*H*-pyran (**35**) or 2,3-dihydrofuran (**32**) (Scheme 5). In this reaction, imine **16** is the diene and with **35** gave the product **36** in 16% yield. Only the *trans*-diastereomer **36** was found. The yield increased to 70% when **32** was used as the dienophile. However, both possible diasteremomers **33** and **34** were formed in a ratio of 1 : 1 as determined by ^{1}H NMR spectroscopy.

The mechanism of the reaction can be considered similar to metal Lewis acid catalysed reactions. The imidazolinium cations, which are Lewis acids, are activating the imines, which react with Danishefsky's diene (**15**) in a [4 + 2] reaction. Intermediates, which can be observed in a Mannich-type condensation mechanism, were not detected during the course of the reaction.

In conclusion, we have demonstrated for the first time that imidazolinium salts are good catalysts for an aza-Diels–Alder reaction with Danishefsky's diene (**15**). The salts are metal-free Lewis acids, which can contribute to the field of organocatalysis. In addition, new imidazolinium salts have been prepared, of

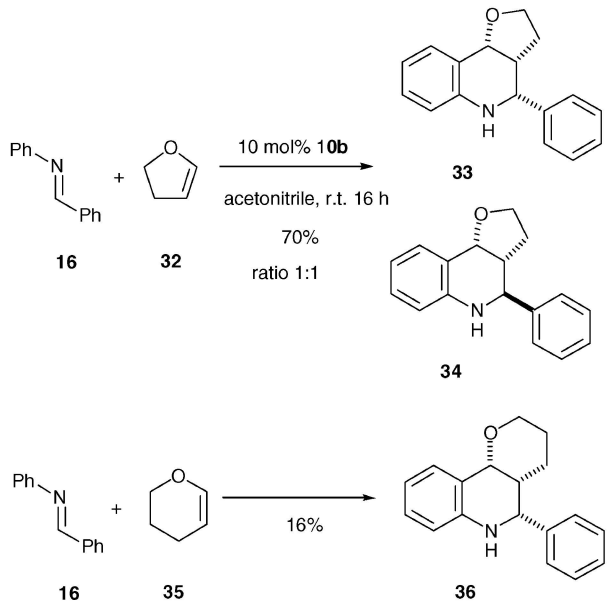


Scheme 4

Table 3 Aza-Diels–Alder reaction with various imines[a]

Run	Imine	R_1	R_2	Product	Yield (%)[b]
1	**16**	C_6H_5	C_6H_5	**17**	95
2	**18**	4-Cl–C_6H_4	C_6H_5	**19**	84
3	**20**	4-MeO–C_6H_4	C_6H_5	**21**	92
4	**22**	C_6H_5	4-Cl–C_6H_4	**23**	72
5	**24**	C_6H_5	2-MeO–C_6H_4	**25**	57
6	**26**	C_6H_5	2-C_5H_4N	**27**	93
7	**28**	C_6H_5	4-MeO–C_6H_4	**29**	45
8	**30**	C_6H_5	4-NO_2–C_6H_4	**31**	50

[a] See Experimental for details. [b] Isolated yields.



Scheme 5

which a few are ionic liquids. Present investigations within the group concern the behaviour of chiral analogues of these salts.

Experimental

General

Imidazolidines **1**, **3**, **5**, **7**, **9**, **11** and **13** were prepared according to a literature procedure.[37] Imines **16**, **18**, **20**, **22**, **24**, **26**, **28** and **30** were prepared according to a literature procedure.[44] 3,4-Dihydro-2*H*-pyran (**35**) and Danishefsky's diene (**15**) were purchased from Merck. 2,3-Dihydrofuran (**32**), anhydrous DME and $LiN(CF_3SO_2)_2$ were purchased from Aldrich. KPF_6 was purchased from Fluka and *N*-bromoacetamide was purchased from Lancaster. Reactions were carried out under nitrogen and were performed using standard Schlenk line techniques.[45] Acetonitrile and DCM were distilled from calcium hydride. Toluene was distilled from sodium.

Flash column chromatography[46] was performed on Sorbisil C-60. All reactions were monitored by TLC with Merck Silica gel 60 F_{254} plates. Elemental analyses were carried out by the Microanalytical Laboratory of the Institut für Pharmazeutische Chemie der Universität Braunschweig. Infrared spectra were recorded on a Perkin–Elmer 2000 FT-IR System. NMR spectra were taken in $CDCl_3$ at ambient temperature on Bruker AMX 400 and a Bruker AC 200F instruments. Mass spectra were recorded on Hewlett Packard 5898B instrument (at 70 eV). Melting points were taken with an apparatus from Dr Tottoli and are uncorrected.

General procedure for the preparation of imidazolinium bromide salts

Imidazolidine (1 mmol) was dissolved in a minimal amount of 1,2-dimethoxyethane. *N*-Bromacetamide (1 mmol) was added in two portions (0.5 mmol each) with an interval of 15 min. After addition of the second portion, the reaction mixture was stirred for an additional hour. The salt precipitated and was isolated by filtration. In cases where no precipitate was formed, diethyl ether was added and an oily solid formed. The solvent was decanted and the residue was washed with diethyl ether and dried under high vacuum to give the corresponding bromide salt. This procedure is a modification of a literature procedure.[38]

1,3-Dibenzyl-2-(phenyl)imidazolinium bromide (2a). From **1** in 95% yield as a white hygroscopic solid, m.p. 167 °C. MS (EI), *m/e* 326 (cation $M^+ - H$, 75%), 249 (45), 234 (50), 132 (25), 91 (100); IR (KBr) 3442s, 1601vs, 1581s, 1569s 1253s, 726s, 699s cm^{-1}; ^1H NMR (400 MHz) δ 8.04–8.02 (m, 2 H, H-14,18), 7.71–7.66 (m, 3 H, H-15,16,17), 7.42–7.23 (m, 10 H, H–Ar), 4.57 (s, 4 H, H-6,19), 4.13 (s, 4 H, H-4,5); ^{13}C NMR (100 MHz) δ 167.4, 133.4, 133.2, 130.5, 129.7, 129.32, 129.28, 128.6, 122.6, 52.7, 48.7.

1,3-Dibenzyl-2-(2-chlorophenyl)imidazolinium bromide (4a). From **3** in 93% yield as a yellow hygroscopic oil. MS (EI), *m/e* 360 (cation $M^+ - H$, 30%), 269 (50), 151 (30), 91 (100); IR (neat) 3355s, 3177s, 1664vs, 1598vs, 1291s, 1254s, 759s, 703s cm^{-1}; ^1H NMR (400 MHz) δ 8.95–8.92 (m, 1 H, H-15), 7.69–7.61 (m, 3 H, H–Ar), 7.43–7.35 (m, 10 H, H–Ar), 4.64 (d, J = 15.1 Hz, 2 H, H-6,19), 4.52–4.47 (m, 2 H, H-4,5), 4.42 (d, J = 14.8 Hz, 2 H, H-6,19), 3.77–3.72 (m, 2 H, H-4,5); ^{13}C NMR (100 MHz) δ 164.1, 134.7, 133.6, 132.4, 132.0, 130.6, 129.7, 126.44, 129.36, 129.1, 122.2, 52.7, 48.6.

1,3-Dibenzyl-2-(4-chlorophenyl)imidazolinium bromide (6a). From **5** in 88% yield as a white hygroscopic solid, m.p. 155 °C. MS (EI), *m/e* 360 (cation $M^+ - H$, 15%), 269 (40), 151 (40), 91 (100); IR (KBr) 3026m, 2996m, 1605vs, 1581s, 1565s, 1482s, 1253s, 834s, 707vs cm^{-1}; ^1H NMR (400 MHz) δ 8.05–8.02 (m, 2 H, H-15,17), 7.65–7.63 (m, 2 H, H-14,18), 7.39–7.35 (m, 6 H, H–Ar), 7.25–7.22 (m, 4 H, H–Ar), 4.56 (s, 4 H, H-6,19), 4.12 (s, 4 H, H-4,5); ^{13}C NMR (100 MHz) δ 166.6, 140.1, 132.9, 130.9, 129.8, 129.4, 128.5, 120.9, 77.7, 52.7, 48.8.

1,3-Dibenzyl-2-(2,4-dichlorophenyl)imidazolinium bromide (8a). From **7** in 91% yield as a yellow hygroscopic oil. MS (EI), *m/e* 394 (cation $M^+ - H$, 10%), 304 (10), 185 (15), 91 (100), 65 (20); IR ($CDCl_3$) 2360s, 1600vs, 1455m, 910vs, 730vs cm^{-1}; ^1H NMR (400 MHz) δ 9.10 (d, J = 8.4 Hz, 1 H, H-15), 7.68–7.62 (m, 2 H, H-17,18), 7.47–7.35 (m, 10 H, H–Ar), 4.65 (d, J = 14.8 Hz, 2 H, H-6,19), 4.52–4.47 (m, 2 H, H-4,5), 4.41 (d, J = 14.8 Hz,

2 H, H-6,19), 3.75–3.70 (m, 2 H, H-4,5); ^{13}C NMR (100 MHz) δ 163.4, 140.7, 134.9, 132.9, 132.3, 130.6, 130.0, 129.7, 129.4, 129.1, 120.7, 52.8, 48.7.

1,3-Dibenzyl-2-(pentafluorophenyl)imidazolinium bromide (10a). From **9** in 90% yield as a yellow hygroscopic oil. MS (EI), *m/e* 417 (cation M$^+$, 1%), 326 (5), 235 (5), 207 (5), 91 (100); IR (neat) 1665vs, 1605vs, 1518s, 1365s, 12995s, 998s cm^{-1}; ^{1}H NMR (200 MHz) δ 7.41–7.19 (m, 10 H, H–Ar), 4.71 (s, 4 H, H-16,19), 4.37 (s, 4 H, H-4,5); ^{13}C NMR (50 MHz) δ 172.9, 131.0, 129.5, 128.4, 52.6, 49.4.

1,3-Dibenzyl-2-(2-pyridinyl)imidazolinium bromide (12a). From **11** in 99% yield as a colorless hygroscopic oil. MS (EI), *m/e* 328 (cation M$^+$, 20%), 237 (30), 105 (35), 91 (100), 78 (35), 65 (35), 51 (35); IR ($CDCl_3$) 1668m, 1601s, 910vs, 732vs, 650s cm^{-1}; ^{1}H NMR (400 MHz) δ 8.97 (d, J = 8.3 Hz, 1 H, H-15,), 7.63–7.59 (m, 2 H, H-17,18), 7.38–7.27 (m, 11 H, H–Ar), 4.50 (d, J = 14.9 Hz, 2 H, H-6,19), 4.44–4.35 (m, 4 H, H-4,5,6,19), 3.73–3.68 (m, 2 H, H-4,5); ^{13}C NMR (100 MHz) δ 163.4, 140.8, 134.6, 132.9, 132.2, 130.7, 129.9, 129.7, 129.4, 129.1, 52.8, 48.7.

1,3-Dibenzyl-2-(2-thiophenyl)imidazolinium bromide (14a). From **13** in 90% yield as a white solid, m.p. 157 °C. MS (EI), *m/e* 332 (cation M$^+$ − H, 10%), 241 (30), 123 (30), 91 (100), 65 (20); IR (KBr) 1593s, 1577s, 1287m, 761m, 733m cm^{-1}; ^{1}H NMR (400 MHz) δ 8.17–8.15 (m, 1 H, H-2), 7.81 (dd, J = 6.8 Hz, J = 1.24 Hz), 7.40–7.28 (m, 11 H, H–Ar), 4.69 (s, 4 H, H-11,18), 4.08 (s, 4 H, H-8,9); ^{13}C NMR (100 MHz) δ 162.9, 135.9, 133.1, 132.9, 129.7, 129.5, 129.3, 128.6, 119.7, 53.1, 48.7.

General procedure for counter-anion exchange with potassium hexafluorophosphate

Imidazolinium bromide (1 mmol) was dissolved in DCM (3 ml) and stirred vigorously with 1.5 equiv. of KPF_6 in water (3 ml) for 30 minutes. The organic phase was separated, washed with water (3 × 3 ml) and dried with 3 Å molecular sieves. The solvent was evaporated and the product was further dried overnight under high vacuum to give the corresponding imidazolinium hexafluorophosphate.

1,3-Dibenzyl-2-(2-phenyl)imidazolinium hexafluorophosphate (2b). From **2a** in 86% yield as a yellow solid, m.p. 118 °C. MS (EI), *m/e* 326 (cation M$^+$ − H, 75%), 249 (45), 234 (50), 132 (25), 91 (100); IR (KBr) 1598vs, 1441m, 1355m, 1301m 1252s, 839vs, 774s, 763s, 703s cm^{-1}; ^{1}H NMR (400 MHz) δ 7.75–7.65 (m, 5 H, H–Ar), 7.43–7.16 (m, 10 H, H–Ar), 4.48 (s, 4 H, H-6,19), 3.98 (s, 4 H, H-4,5); ^{13}C NMR (100 MHz) δ 167.0, 133.6, 132.8, 130.8, 129.8, 129.4, 128.7, 128.4, 122.2, 52.2, 48.0; Anal. calculated for $C_{23}H_{23}N_2PF_6$: C, 58.48; H, 4.91; N, 5.93, found: C, 58.48; H, 4.91; N, 5.78.

1,3-Dibenzyl-2-(2-chlorophenyl)imidazolinium hexafluorophosphate (4b). From **4a** in 95% yield as a yellow solid, m.p. 144 °C. MS (EI), *m/e* 360 (cation M$^+$ − H, 70%), 324 (40), 283 (20), 91 (100); IR (KBr) 1598vs, 1441m, 1355m, 1301m 1252s, 839vs, 774s, 763s, 703s cm^{-1}; ^{1}H NMR (400 MHz) δ 8.09–8.07 (m, 1 H, H-15), 7.76–7.68 (m, 3 H, H–Ar), 7.44–7.27 (m, 10 H, H–Ar), 4.49–4.39 (m, 4 H, H-6,19), 4.22–4.17 (m, 2 H, H-4,5), 3.84–3.79 (m, 2 H, H-4,5); ^{13}C NMR (100 MHz) δ 163.9, 135.0, 132.3, 132.0, 131.8, 131.0, 129.8, 129.63, 129.59, 129.0, 121.0, 52.3, 48.1. Anal. calculated for $C_{23}H_{22}ClN_2PF_6$: C, 54.50; H, 4.37; N, 5.53, found: C, 54.57; H, 4.22; N, 5.40.

1,3-Dibenzyl-2-(4-chlorophenyl)imidazolinium hexafluorophosphate (6b). From **6a** in 89% yield as a white solid, m.p. 71 °C. MS (EI), *m/e* 361 (cation M$^+$, 5%), 270 (10), 151 (15), 107 (15), 91 (100), 55 (60); IR (KBr) 1602vs, 1565s, 1456s, 1360s, 1288s, 1095s, 834vs, 749s, 702s cm^{-1}; ^{1}H NMR (400 MHz) δ 8.05–8.02 (m, 2 H, H-15,17), 7.65–7.63 (m, 2 H, H-14,18), 7.39–7.35 (m, 6 H, H–Ar), 7.25–7.22 (m, 4 H, H–Ar), 4.56 (s, 4 H, H-6,19), 4.12 (s, 4 H, H-4,5); ^{13}C NMR (100 MHz) δ 166.6, 140.1, 132.9, 130.9, 129.8, 129.4, 128.5, 120.9, 77.7, 52.7, 48.8. Anal. calculated for $C_{23}H_{22}ClF_6N_2P$: C, 54.50; H, 4.37; N, 5.53, found: C, 54.31; H, 4.09; N, 5.37.

1,3-Dibenzyl-2-(2,4-dichlorophenyl)imidazolinium hexafluorophosphate (8b). From **8a** in 90% yield as a yellow solid, m.p. 130 °C. MS (EI), *m/e* 394 (cation M$^+$ − H, 50%), 358 (40), 317 (20), 282 (20), 91 (100), 65; IR (KBr) 3095m, 1599vs, 1254s, 840vs, 702s, 557s cm^{-1}; ^{1}H NMR (400 MHz) δ 8.01 (d, 1 H, J = 8.4 Hz, H-15), 7.70–7.69 (m, 1 H, H-17), 7.65–7.22 (m, 1 H, H-18), 7.42–7.36 (m, 6 H, H–Ar), 7.28–7.24 (m, 4 H, H–Ar), 4.46–4.37 (m, 4 H, H-6,19), 4.17–4.12 (m, 2 H, H-4,5), 3.85–3.80 (m, 2 H, H-4,5); ^{13}C NMR (100 MHz) δ 163.1, 141.1, 133.3, 132.6, 131.8, 131.1, 130.1, 129.8, 129.6, 129.0, 120.3, 52.3, 48.2. Anal. calculated for $C_{23}H_{21}Cl_2N_2PF_6$: C, 51.03; H, 3.91; N, 5.18, found: C, 50.73; H, 3.81; N, 4.86.

1,3-Dibenzyl-2-(pentafluorophenyl)imidazolinium hexafluorophosphate (10b). From **10a** in 90% yield as a white solid, m.p. 161 °C. MS (ESI), *m/e* 417.1 (cation M$^+$, 100%); IR (KBr) 1610m, 1520m, 840s cm^{-1}; ^{1}H NMR (400 MHz) δ 7.40–7.18 (m, 10 H, H–Ar), 4.54 (s, 4 H, H-6,19), 4.08 (s, 4 H, H-4,5); ^{13}C NMR (100 MHz) δ 155.1, 131.3, 129.9, 128.7, 52.7, 48.9. Anal. Calcd for $C_{23}H_{18}N_2PF_{11}$ C, 49.12; H, 3.23; N, 4.98. Found: C, 49.07; H, 3.51; N, 4.81.

1,3-Dibenzyl-2-(2-pyridinyl)imidazolinium hexafluorophosphate (12b). From **12a** in 71% yield as white solid, m.p. 120 °C. MS (EI), *m/e* 327 (cation M$^+$ − H, 30%), 236 (30), 105 (20), 91 (100), 65 (20); IR (KBr) 1619m, 1599m, 839s, 557m cm^{-1}; ^{1}H NMR (400 MHz) δ 8.94 (d, J = 4.7 Hz, 1 H, H-15), 8.21 (d, J = 7.6 Hz, 1 H, H-17), 8.14–8.10 (m, 1 H, H-18), 7.71–7.68 (m, 1 H, H-16), 7.44–7.32 (m, 10 H, H–Ar), 4.50 (s, 4 H, H-6,19), 4.00 (s, 4 H, H-4,5); ^{13}C NMR (100 MHz) δ 163.8, 151.6, 142.2, 139.2, 132.6, 129.7, 129.5, 128.8, 127.8, 126.9, 52.9, 48.8. Anal. calculated for $C_{22}H_{22}F_6N_3P$: C, 55.82; H, 4.68; N, 8.88, found: C, 55.97; H, 4.63; N, 8.57.

1,3-Dibenzyl-2-(2-thiophenyl)imidazolinium hexafluorophosphate (14b). From **14a** in 92% yield as a white solid, m.p. 110–112 °C. MS (EI), *m/e* 332 (cation M$^+$ − H, 20%), 240 (30), 132 (20), 91 (100), 65 (20); IR (KBr) 1596s, 1580s, 1283m, 836vs, 731m, 698m cm^{-1}; ^{1}H NMR (400 MHz) δ 7.86–7.82 (m, 2 H, H-2,3), 7.44–7.34 (m, 7 H, H–Ar), 7.28–7.25 (m, 4 H, H–Ar), 4.61 (s, 4 H, H-11,18), 3.98 (s, 4 H, H-8,9); ^{13}C NMR (100 MHz) δ 162.3, 135.2, 133.3, 132.8, 129.83, 129.80, 129.4, 128.4, 119.1, 52.6, 48.1. Anal. calculated for $C_{21}H_{21}N_2SPF_6$: C, 52.72; H, 4.42; N, 5.86, found: C, 52.36; H, 4.39; N, 5.68.

General procedure for counter-anion exchange with lithium bis-(trifluoromethylsulfonyl)imide

Imidazolinium bromide (1 mmol) was dissolved in DCM (3 ml) and vigorously stirred with a solution of $LiN(CF_3SO_2)_2$ (1.5 mmol) in water (3 ml) for 30 minutes. The organic phase was separated, washed with water (3 × 3 ml) and dried with molecular 3 Å sieves. The solvent was evaporated and the product was further dried under high vacuum overnight to give the corresponding imidazolinium bis(trifluromethylsulfonyl)imide.

1,3-Dibenzyl-2-(2-chlorophenyl)imidazolinium bis(trifluoromethylsulfonyl)imide (4c). From **4a** in 71% yield as a white solid, m.p. 83 °C. MS (EI), *m/e* 360 (cation M$^+$ − H, 100%), 151 (5), 91 (60); IR (KBr) 1604vs, 1471m, 1458m, 1441m, 1355vs, 1304s, 1192vs, 1135s, 1056s, 772s, 702s, 616s cm^{-1}; ^{1}H NMR (400 MHz) δ 8.09–8.07 (m, 1 H, H-15), 7.76–7.70 (m, 3 H, H–Ar), 7.45–7.40 (m, 4 H, H–Ar), 7.30–7.27 (m, 6 H, H–Ar), 4.50–4.39 (m, 4 H, H-6,19), 4.24–4.19 (m, 2 H, H-4,5), 3.80–3.75 (m, 2 H, H-4,5); ^{13}C NMR (100 MHz) δ 163.8, 135.0, 132.2, 131.9, 131.0, 129.8, 129.69, 129.66, 129.1, 121.9, 77.7, 52.3, 47.9. Anal. calculated for $C_{25}H_{22}ClF_6N_3O_4S_2$: C, 46.77; H, 3.45; N, 6.54, found: C, 46.45; H, 3.34; N, 6.57.

1,3-Dibenzyl-2-(4-chlorophenyl)imidazolinium bis(trifluoromethylsulfonyl)imide (6c). From **6a** in 90% yield as a white solid, m.p. 80 °C. MS (EI), *m/e* 360 (cation $M^+ - H$, 100%), 227 (70), 152 (70), 89 (70), 77 (40); IR (KBr) 1596s, 1563m, 1354s, 1289m, 1289m, 1227s, 1203vs, 1182m, 1063s, 703m, 614s cm^{-1}; ^1H NMR (400 MHz) δ 7.76–7.68 (m, 4 H, H-14,15,17,18), 7.46–7.38 (m, 6 H, H–Ar), 7.23–7.21 (m, 4 H, H–Ar), 4.50 (s, 4 H, H-6,19), 4.00 (s, 4 H, H-4,5); ^{13}C NMR (100 MHz) δ 166.3, 140.5, 132.5, 131.2, 130.3, 129.9, 129.5, 128.4, 121.0, 120.4, 118.8, 52.3, 48.1. Anal. calculated for $C_{25}H_{22}ClF_6N_3O_4S_2$: C, 46.77; H, 3.45; N, 6.54, found: C, 46.46; H, 3.42; N, 6.38.

General procedure for the catalysed aza-Diels–Alder reaction in acetonitrile

The imine (0.2 mmol) and the catalyst (0.02 mmol, 10 mol%) were placed into a dry Schlenk flask under nitrogen. The reaction mixture was dissolved in dry acetonitrile (2 ml) and Danishefsky's diene (**15**) (0.22 mmol, 42.8 µl) was added. After 16 h stirring at room temperature, the mixture was quenched by addition of a saturated solution of potassium hydrogencarbonate (2 ml) and extracted with ethyl acetate (3 × 5 ml). Organic phases were combined, dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. Flash column chromatography (PE–EtOAc, 1 : 1) gave the desired product.

2,3-Dihydro-1,2-diphenylpyridin-4(1*H*)-one (17). From **15** and **16** in 95% yield as a yellow solid, m.p. 53 °C (lit.[47] m.p. 54–55 °C). Spectral data were consistent with literature values.[35]

1-(4-Chlorophenyl)-2,3-dihydro-2-phenylpyridin-4(1*H*)-one (19). From **15** and **18** in 84% yield as a yellow solid, m.p. 148 °C (lit.[33] m.p. 150 °C). Spectral data were consistent with literature values.[33]

1-(4-Methoxyphenyl)-2,3-dihydro-2-phenylpyridin-4(1*H*)-one (21). From **15** and **20** in 92% yield as a yellow oil. Spectral data were consistent with literature values.[33]

2,3-Dihydro-2-(4-chlorophenyl)-1-phenylpyridin-4(1*H*)-one (23). From **15** and **22** in 72% yield as an oil. Spectral data were consistent with literature values.[35]

2,3-Dihydro-2-(2-methoxyphenyl)-1-phenylpyridin-4(1*H*)-one (25). From **15** and **24** in 57% yield as an oil. Spectral data were consistent with literature values.[30]

2,3-Dihydro-2-(2-pyridinyl)-1-phenylpyridin-4(1*H*)-one (27). From **15** and **26** in 93% yield as a yellow oil. Spectral data were consistent with literature values.[35]

2,3-Dihydro-2-(4-methoxyphenyl)-1-phenylpyridin-4(1*H*)-one (29). From **15** and **28** in 45% yield as a yellow oil. Spectral data were consistent with literature values.[35]

2,3-Dihydro-2-(4-nitrophenyl)-1-phenylpyridin-4(1*H*)-one (31). From **15** and **30** in 50% yield as a yellow solid, m.p. 155 °C. Spectral data were consistent with literature values.[35]

General procedure for the reversed aza-Diels–Alder reaction

The imine **16** (0.2 mmol) and catalyst **10b** (0.02 mmol, 10 mol%) were placed into a dry Schlenk flask under nitrogen. The reaction mixture was dissolved in dry acetonitrile (2 ml) and the dienophile (2,3-dihydrofuran (**32**) (0.4 mmol, 30.27 µl) or 3,4-dihydro-2*H*-pyran (**34**) (0.4 mmol, 36.18 µl)) was added. After 16 h stirring at room temperature, the solvent was evaporated under reduced pressure. Flash column chromatography (PE–EtOAc, 8 : 2) gave the desired product.

2,3,3a,4,5,9b-Hexahydro-4-phenylfuro[3,2-*c*]quinoline (33) and (34). From **16** and **32** in 70% yield as a 1 : 1 mixture of the diastereomers **33** and **34**. Spectral data were consistent with literature values.[48]

***Trans*-3,4,4a,5,6,10b-hexahydro-5-phenyl-2*H*-pyrano[3,2-*c*]-quinoline (36).** From **16** and **35** in 16% yield as a yellow oil. Spectral data were consistent with literature values.[26]

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The preparation of new enantiopure imidazolinium salts and their evaluation as catalysts and shift reagents

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Abstract—A series of new chiral imidazolinium salts were prepared and tested as catalysts. It was possible to show that bis-imidazolinium salts had a higher reactivity than mono-imidazolinium salts. In addition a chiral discrimination of the bis-imidazolinium salts with the potassium salt of racemic Mosher's acid was proven by NMR studies.

1. Introduction

Recently, a few examples of chiral imidazolinium based ionic liquids have been reported.[1,2] However, the number of examples of this class of chiral ionic liquid remains small compared to other types of chiral ionic liquid.[3–5] Furthermore, we have shown that an achiral imidazolinium based ionic liquid is an inert medium for reactions involving medium and strong bases.[6] Chiral imidazolinium salts, which have a hydrogen atom on the C-2 position and a hydroxyl group incorporated were shown to be shift reagents for the racemic potassium salt of Mosher's acid.[2]

Due to the positive charge delocalized between the two nitrogen atoms and the C-2 carbon atom, the imidazolinium cation can act as a mild Lewis acid. It has been demonstrated that achiral imidazolinium salts are able to catalyze an aza Diels–Alder reaction or inverse electron demand aza Diels–Alder reaction,[7] which is one of the few examples of carbocation based Lewis acids in catalysis.[8–13] Due to the absence of a metal, these salts can contribute to the field of organocatalysis, which has attracted much interest in recent years.[14,15]

Herein, we report the preparation of a series of new chiral imidazolinium salts and their investigation as chiral metal-free Lewis acids and chiral shift reagents. In addition some of the salts presented also qualify as ionic liquids.[16]

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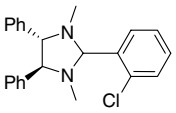
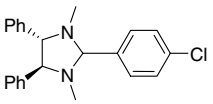
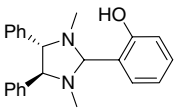
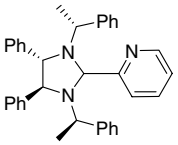
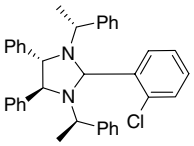
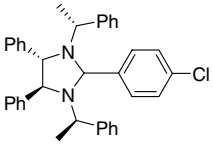
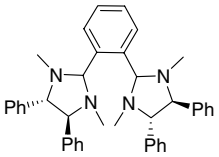
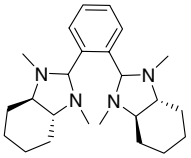
2. Results and discussion

2.1. Preparation

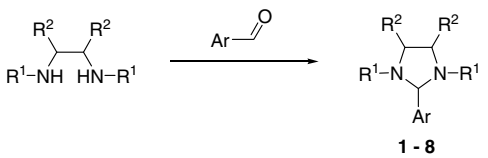
The first step was preparation of the appropriate enantiopure imidazolidines, which were used as the precursors of the desired chiral imidazolinium salts. The imidazolidines, bearing different substituents on the C-2 atom, were formed from chiral diamines and aldehydes (Table 1, Scheme 1). A convenient method to prepare aminals is the use of water as a solvent without the presence of a catalyst, which has recently been described by our group.[17] However, we found that some of the more complex chiral aminals were not formed by applying this procedure, probably due to a certain level of steric hindrance in the chiral diamines.

Therefore, we initially used a standard procedure, Dean–Stark/benzene/reflux,[18] in order to obtain the desired imidazolinium precursors (Table 1, entries 1, 2, 4 and 5). Over the course of our investigation we found that it was also possible to react the diamines with aldehydes under neat conditions in a sealed vessel at 120 °C, without the presence of a catalyst. The aminals were obtained in good to excellent yields (Table 1, entries 3 and 6). Moreover, it was possible to prepare bis-aminals from (−)-(1*S*,2*S*)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethylendiamine[19] or (+)-(1*R*,2*R*)-*N*,*N*′-dimethylcyclohexane-1,2-diamine[19] with phthaldialdehyde in excellent yields (Table 1, entries 7 and 8) under these conditions. However, when (1*S*,2*S*)-1,2-di-*tert*-butyl-*N*,*N*′-bis((*R*)-1-phenylethyl)ethane-1,2-diamine[20] was treated with phthaldialdehyde under neat conditions, no product

Table 1. Preparation of aminals

Entry	Diamine	Aldehyde	Method[a]	Aminal		Yield (%)
1	R^1 = Me, (*R*,*R*)-R^2 = Ph	2-Chlorobenzaldehyde	A		**1**	93
2	R^1 = Me, (*S*,*S*)-R^2 = Ph	4-Chlorobenzaldehyde	A		**2**	91
3		2-Hydroxybenzaldehyde	B		**3**	95
4	R^1 = (*R*)-MeBn, (*S*,*S*)-R^2 = Ph	Pyridine-2-carbaldehyde	A		**4**	95
5		2-Chlorobenzaldehyde	A		**5**	50
6		4-Chlorobenzaldehyde	B		**6**	77
7	R^1 = Me, (*S*,*S*)-R^2 = Ph	Phthaldialdehyde	B		**7**	87
8	R^1 = Me, (*R*,*R*)-R^2 = $(CH_2)_4$	Phthaldialdehyde	B		**8**	99
9	R^1 = (*R*)-MeBn, (*S*,*S*)-R^2 = ^{t}Bu	Phthaldialdehyde	B	—	**9**	0

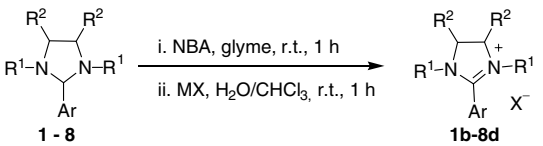
[a] Method A: Dean–Stark/benzene/reflux/24 h; method B: neat, 120 °C, 3 h.



Scheme 1. Preparation of aminals.

could be isolated (Table 1, entry 9). This may be due to the bulky *t*-butyl groups that are incorporated in the diamine.

The aminals were then transformed into the corresponding imidazolinium salts by applying a modified literature procedure.[21] The imidazolidines were oxidized with *N*-bromoacetamide (NBA) to the imidazolinium bromide salts (Scheme 2, Table 2), which were used directly in a counter anion exchange. In some cases, the bromide salts were isolated to confirm by NMR, that the bromide salt was



Scheme 2. Preparation of imidazolinium salts.

Table 2. Oxidation of aminals and counter anion exchange

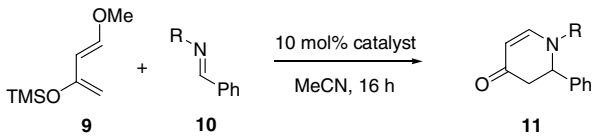
Entry	Aminal	Anion	Salt	Yield (%)
1	*ent*-**1**	PF_6^-	*ent*-**1b**	88
2	**1**	NTf_2^-	**1c**	58
3	**2**	Br^-	**2a**	99
4	**2**	NTf_2^-	**2c**	82
5	**2**	$B[3,5\text{-}(CF_3)_2\text{-}C_6H_3]_4^-$	**2d**	71
6	**4**	Br^-	**4a**	96
7	**4**	PF_6^-	**4b**	86
8	**4**	NTf_2^-	**4c**	57
9	**5**	Br^-	**5a**	89
10	**5**	PF_6^-	**5b**	94
11	**6**	PF_6^-	**6b**	72
12	**7**	NTf_2^-	**7c**	80
13	**7**	$B[3,5\text{-}(CF_3)_2\text{-}C_6H_3]_4^-$	**7d**	80
14	**8**	PF_6^-	**8b**	75
15	**8**	$B[3,5\text{-}(CF_3)_2\text{-}C_6H_3]_4^-$	**8d**	87

obtained in good purity and that all aminal was consumed (Table 2, entries 3, 6 and 9). The bromide salts were difficult to handle, due to their considerable hygroscopic behaviour. Bis-imidazolinium salts were prepared from the bis-aminals **7** and **8** in very good yields (Table 2, entries 12–15).

The counter anion exchange was performed by vigorous stirring of the imidazolinium bromide salt with the metal salt of the new desired anion in a $CHCl_3/H_2O$ mixture. The new imidazolinium salts remained in the organic phase, while the metal bromide salts were removed by washing the organic phase with water. Also, bis-imidazolinium salts **7c** and **8b** could be prepared in good yields following this procedure (Table 2, entries 12 and 15). Salts **6b** and **7d** could qualify as ionic liquids, since their melting points were below 100 °C.[16] Salts **1c**, **4a** and **4c** could qualify as room temperature ionic liquids.

2.2. Investigation of catalytic behaviour

2.2.1. Aza Diels–Alder reaction. Chiral salts *ent*-**1b**–**8d** were tested in the aza Diels–Alder reaction (Scheme 3). A few selected examples are presented in Table 3. In general, the salts showed good catalytic activity, however, no asymmetric induction was observed. When a tosyl substituent



Scheme 3. Aza Diels–Alder reaction.

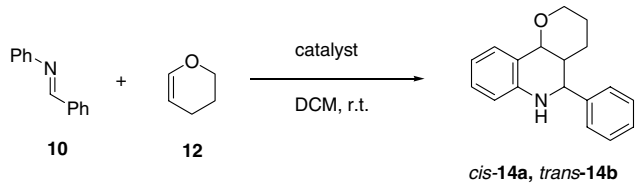
Table 3. Aza Diels–Alder reaction

Entry	Catalyst	R	T (°C)	Yield (%)
1	**5b**	Ph	0	76
2	**5b**	Ph	rt	82
3	**4b**	Ph	0	78
4[a]	**4b**	Ts	rt	35

[a] Reaction was performed in DCM.

was present on the imine nitrogen atom, a lower reactivity was observed, and no enantioselectivity was found (Table 3, entry 4).

2.2.2. Inverse electron demand aza Diels–Alder reaction. We then explored the enantiopure salts in the inverse electron demand aza Diels–Alder reaction of *N*-benzylideneaniline **10** and dihydropyran **12** (Scheme 4).



Scheme 4. Inverse electron demand aza Diels–Alder reaction.

The reaction with dihydropyran **12** and **10** was not sufficiently catalyzed by the mono-imidazolinium salts. For example, when 10 mol % of salt **6b** was used as the catalyst, only traces of the desired product were obtained after 72 h at rt. Bis-imidazolinium salt **7c** revealed a poor reactivity and **14a** and **14b** were isolated in 6% yield in a ratio of 58:42 after 112 h at rt. However, when salt **7d**, which incorporated the very lipophilic and large anion $B[3,5\text{-}(CF_3)_2\text{-}C_6H_3]_4^-$, was applied, the reactivity increased dramatically and **14a** and **14b** were obtained in 64% yield with a ratio of 54:46 after 16 h at rt. Both diastereomers were obtained as racemates. In addition, the bis-imidazolinium salt **8d** resulted in a yield of 67% after 96 h at 0 °C in a diastereomeric ratio of 60:40 for **14a** and **14b**. No enantiomeric excess was found.

2.3. Use as a shift reagent

Mono-imidazolinium salts bearing a hydrogen atom at the C-2 position and a hydroxy group on the side chain have been shown to be shift reagents for a racemate of potassium Mosher's carboxylate.[2] To the best of our knowledge, no imidazolinium salts with an aryl substituent at the C-2 position have been investigated as shift reagents. When

Table 4. Chemical shifts of Mosher's carboxylate in ppm and $\Delta\delta$ in Hz on a 400 MHz NMR

Entry	Salt	^1H $\delta(S)$	^1H $\delta(R)$	^{19}F $\delta(S)$	^{19}F $\delta(R)$	^1H $\Delta\delta$	^{19}F $\Delta\delta$
1	**8b**	3.59	3.57	−71.50	−71.64	6.3	53.0
2	**8d**	3.57	3.57	−71.67	−71.72	0	18.8
3	**7d**	3.58	3.60	−71.57	−71.49	4.3	27.1
4	**7c**	3.57	3.57	−71.84	−71.88	0	13.0

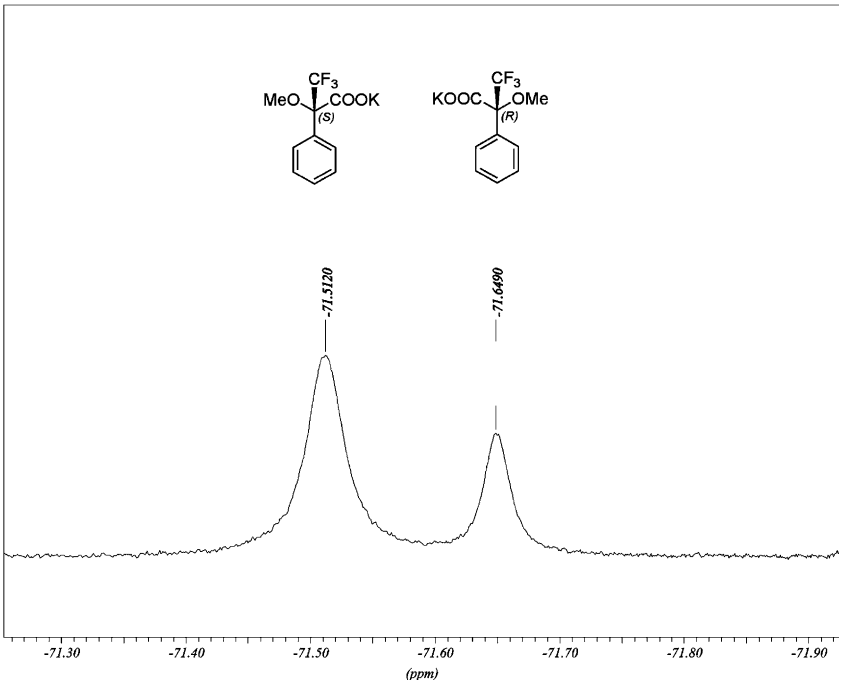


Figure 1. ^{19}F NMR spectra on a 400 MHz NMR measured at 375 MHz.

the mono-imidazolinium salts were applied, no splitting of either the ^{1}H or ^{19}F signal of Mosher's carboxylate was observed. However, the bis-imidazolinium salts **8b**, **8d**, **7d** and **7c** were able to divide the ^{19}F signal of the two enantiomers as shown in Table 4. Only **8b** and **7d** were also able to split the ^{1}H signal. The best result for an ^{19}F NMR with salt **8b** is depicted in Figure 1. In this example, an enantioenriched sample of 50% ee of Mosher's carboxylate was used, in order to assign the individual NMR signals to either the (*R*)- or (*S*)-enantiomer through integration.

3. Conclusion

In conclusion, we have prepared a range of new chiral mono- and bis-imidazolinium salts. It was shown that the bis-imidazolinium salts were far more active catalysts, however, no asymmetric induction was found in the test reactions. In addition, it was demonstrated that the bis-imidazolinium salts can be used as a shift reagent for the potassium salt of Mosher's acid.

4. Experimental

4.1. General experimental

Flash column chromatography[22] (FCC) was performed on Sorbisil C-60. The reactions were monitored by TLC with Merck Silica gel 60 F_{254} plates. Elemental analyses were carried out by the Microanalytical Laboratory of the Institut für Pharmazeutische Chemie der Technischen Universität Braunschweig. Infrared spectra were recorded on a Bruker Vector 22 FTIR instrument. NMR spectra were performed at ambient temperature on a Bruker AMX 400 and a Bruker AC 200F and, if not otherwise stated, measured in $CDCl_3$. Mass spectra were recorded on Hewlett–Packard 5898B (at 70 eV). Electron spray mass spectrometry was performed directly on a MS LC/MSD 1100 MSD from Hewlett–Packard. High resolution mass spectra were recorded at the Institute of Organic Chemistry, University of Hanover. Melting points are uncorrected. Reactions were performed under a nitrogen atmosphere. All solvents were dried using standard procedures, before using in the reactions. Sodium tetrakis(3,5-bis(trifluoromethyl)phenyl)borate,[23] (1*S*,2*S*)-1,2-diphenyl-*N*,*N*′-bis((*R*)-1-phenylethyl)ethane-1,2-diamine,[24] (+)-(1*R*,2*R*)-, (−)-(1*S*,2*S*)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethylendiamine[19] and (+)-(1*R*,2*R*)-*N*,*N*′-dimethylcyclohexane-1,2-diamine[19] were prepared according to the literature procedures. *N*-Bromoacetamide and racemic Mosher's acid were purchased from Lancaster. $LiNTf_2$ and KPF_6 were purchased from Aldrich.

4.2. Preparation of aminals

4.2.1. General procedure for the preparation of aminals (method A). A diamine (1 mmol), *p*-toluenesulfonic acid (5 mg) and an aldehyde (1 mmol) were dissolved in benzene (25 mL). The reaction mixture was refluxed on a Dean–Stark for 24 h. Benzene was removed under reduced pressure to give the crude product, which was purified by FCC (petroleum ether/ethyl acetate/Et_3N, 95/5/0.5) to give the desired aminal.

4.2.2. General procedure for the preparation of aminals under solvent free conditions (method B). A diamine (1 mmol) and an aldehyde (1 mmol) were placed in a pressure vessel equipped with a magnetic stirrer. The vessel was flushed with nitrogen, sealed and the reaction mixture

heated up to 120 °C for 16 h. After cooling to rt, the glassy solid formed was dissolved in DCM and dried over Na_2SO_4. The solvent was removed under reduced pressure and the remaining solid was dried under vacuum to give the corresponding aminal.

4.2.3. (+)-(4*R*,5*R*)-2-(2-Chlorophenyl)-1,3-dimethyl-4,5-diphenylimidazolidine 1. (+)-(4*R*,5*R*)-2-(2-Chlorophenyl)-1,3-dimethyl-4,5-diphenylimidazolidine **1** was prepared from (+)-(*R*,*R*)-*N*,*N*′-dimethyl-1,2-diphenylethylenediamine (500 mg, 2.08 mmol) and *o*-chlorobenzaldehyde (246 μL, 2.18 mmol) in benzene (50 mL) according to method A. FCC gave the *title compound* (+)-**1** as a white solid (700 mg, 93%). Mp 128 °C. $[\alpha]_D^{22} = 107.6$ (*c* 0.59, $CHCl_3$); MS (EI), *m*/*e* 361 (M^+-H, 30%), 244 (40), 243 (100), 208 (40), 152 (25); IR (KBr) 2792s, 1452s, 1263s, 1011s, 756vs, 699vs cm^{-1}; ^1H NMR (200 MHz): δ 8.02–7.98 (m, 1H), 7.43–7.16 (m, 13H), 5.38 (s, 1H, NC*H*N), 3.84 (d, $J = 8.5$ Hz, 2H, C*H*Ph), 3.63 (d, $J = 8.5$ Hz, 2H, C*H*Ph), 2.16 (s, 3H, NCH_3), 1.91 (s, 3H, NCH_3); ^{13}C NMR (50 MHz): δ 139.8, 139.3, 137.5, 130.9, 129.6, 129.1, 128.3, 128.2, 128.1, 128.0, 127.5, 127.4, 126.7, 83.2 (N*C*HN), 37.6 (*C*HPh), 35.6 (NCH_3). Anal. Calcd for $C_{23}H_{23}ClN_2$: C, 76.12; H, 6.39; N, 7.72. Found: C, 76.36; H, 6.26, N, 7.49.

4.2.4. (−)-(4*S*,5*S*)-2-(2-Chlorophenyl)-1,3-dimethyl-4,5-diphenylimidazolidine *ent*-1. (−)-(4*S*,5*S*)-2-(2-Chlorophenyl)-1,3-dimethyl-4,5-diphenylimidazolidine *ent*-**1** was prepared in the same way as the enantiomer above. The spectral data were consistent with the data of **1**.

4.2.5. (−)-(4*S*,5*S*)-2-(4-Chlorophenyl)-1,3-dimethyl-4,5-diphenylimidazolidine 2. (−)-(4*S*,5*S*)-2-(4-Chlorophenyl)-1,3-dimethyl-4,5-diphenylimidazolidine **2** was prepared from (+)-(*S*,*S*)-*N*,*N*′-dimethyl-1,2-diphenylethylenediamine (750 mg, 3.13 mmol) and 4-chlorobenzaldehyde (483 mg, 3.44 mmol) in benzene (50 mL) according to method A. FCC gave the *title compound* (−)-**2** as a white solid (1.029 g, 91%). Mp = 98 °C; $[\alpha]_D^{22} = -35.5$ (*c* 0.32, $CHCl_3$); MS (EI), *m*/*e* 360 (M^+, 40%), 244 (40), 243 (100), 165 (45), 152 (60), 139 (40), 118 (40), 91 (50), 77 (60), 69 (50), 51 (40); IR (KBr) 3425s, 2789s, 1599s, 1490s, 1451s, 1088s, 1009s, 841s, 759s, 698vs, 511s cm^{-1}; ^1H NMR (400 MHz): δ 7.61 (d, $J = 8.6$ Hz, 2H), 7.44 (d, $J = 8.4$ Hz, 2H) 7.37–7.19 (m, 10H), 4.78 (s, 1H, NC*H*N), 3.91 (d, $J = 8.3$ Hz, 1H, C*H*Ph), 3.68 (d, $J = 8.3$ Hz, 1H, C*H*Ph), 2.20 (s, 3H, NCH_3), 1.88 (s, 3H, NCH_3); ^{13}C NMR (100 MHz): δ 140.1, 139.78, 139.73, 134.4, 131.1, 128.8, 128.7, 128.5, 128.3, 127.96, 127.92, 88.2 (N*C*HN), 77.9 (*C*HPh), 37.9 (NCH_3), 36.2 (NCH_3). Anal. Calcd for $C_{23}H_{23}ClN_2$: C, 76.12; H, 6.39; N, 7.72. Found: C, 76.26; H, 6.41; N, 7.73.

4.2.6. (−)-2-((4*S*,5*S*)-1,3-Dimethyl-4,5-diphenylimidazolidin-2-yl)phenol 3. (−)-2-((4*S*,5*S*)-1,3-Dimethyl-4,5-diphenylimidazolidin-2-yl)phenol **3** was prepared from (+)-(*S*,*S*)-*N*,*N*′-dimethyl-1,2-diphenylethylenediamine (608 mg, 2.53 mmol) and salicyl aldehyde (0.264 mL, 2.53 mmol) according to method B as a yellow oil which solidified (830 mg, 95%). Mp 40–42 °C; $[\alpha]_D^{22} = -38.9$ (*c* 0.18, $CHCl_3$); MS (EI), *m*/*e* 343 (M^+-H, 30%), 224 (100), 208 (30), 134 (30), 120 (25), 91 (30); IR (KBr) 2850w, 1619vs, 1480m, 1454m, 1261s, 1152m, 756s, 699s cm^{-1}; ^1H NMR (200 MHz): δ 7.40–7.13 (m, 12H), 6.94–6.84 (m, 2H), 4.84 (s, 1H, NC*H*N), 4.09 (d, $J = 8.7$ Hz, 2H, C*H*Ph), 3.61 (d, $J = 8.7$ Hz, 2H, C*H*Ph), 2.22 (s, 3H, NCH_3), 2.02 (s, 3H, NCH_3); ^{13}C NMR (50 MHz): δ 158.5 (*C*OH), 139.5, 137.2, 131.2, 130.2, 128.7, 128.3, 128.2, 128.1, 127.8, 127.7, 120.7, 119.1, 89.4 (N*C*HN), 36.9 (*C*HPh), 35.6 (NCH_3); HRMS (ESI) calculated for $C_{23}H_{24}N_2O^+$: 345.1967, found: 345.1981.

4.2.7. (+)-(4*S*,5*S*)-2-(2-Pyridinyl)-4,5-diphenyl-1,3-bis((*R*)-1-phenylethyl)imidazolidine 4. (+)-(4*S*,5*S*)-2-(2-Pyridinyl)-4,5-diphenyl-1,3-bis((*R*)-1-phenylethyl)imidazolidine **4** was prepared from (1*S*,2*S*)-1,2-diphenyl-*N*,*N*′-bis((*R*)-1-phenylethyl)ethane-1,2-diamine (1.50 g, 3.57 mmol), 2-pyridinecarbaldehyde (340 μL, 3.57 mmol) and *p*-toluenesulfonic acid (10 mg) in benzene (100 mL) according to method A. The reaction mixture was refluxed for 48 h. FCC gave the *title compound* (+)-**4** as a white solid (1.73 g, 95%). Mp 105–108 °C; $[\alpha]_D^{22} = +115.0$ (*c* 0.32, $CHCl_3$); MS (CI), *m*/*e* 432 (M^+−pyridinyl, 50%), 299 (60), 105 (100); IR (KBr) 3451vs, 1492s, 1453s, 1431s, 1104s, 760s, 699vs cm^{-1}; ^1H NMR (400 MHz): δ 8.57–8.54 (m, 1H), 7.40–7.00 (m, 20H), 6.80–6.70 (m, 3H), 5.34 (s, 1H, NC*H*N), 4.65 (d, $J = 7.9$ Hz, 1H, NC*H*Ph), 4.18 (d, $J = 7.9$ Hz, 1H, NC*H*Ph), 3.98 (q, $J = 7.0$ Hz, 1H, C*H*CH_3), 3.67 (q, $J = 7.0$ Hz, 1H, C*H*CH_3), 1.07 (d, $J = 7.1$ Hz, 3H, CHC*H*$_3$), 0.88 (d, $J = 7.1$ Hz, 3H, CHC*H*$_3$); ^{13}C NMR (100 MHz): δ 165.4, 148.5, 145.4, 143.2, 142.9, 142.5, 135.3, 128.9, 128.6, 128.34, 128.30, 128.28, 128.20, 128.0, 127.4, 127.3, 127.2, 127.1, 127.05, 124.6, 122.0, 83.2 (N*C*HN), 76.6 (*C*HPh), 73.6 (*C*HPh), 61.5 (CH*C*H_3), 57.3 (CH*C*H_3), 23.1 (CH*C*H_3), 22.5 (CH*C*H_3); HRMS (ESI) calculated for $C_{36}H_{35}N_3^+$: 510.2909, found: 510.2912.

4.2.8. (−)-(4*S*,5*S*)-2-(2-Chlorophenyl)-4,5-diphenyl-1,3-bis((*R*)-1-phenylethyl)imidazolidine 5. (−)-(4*S*,5*S*)-2-(2-Chlorophenyl)-4,5-diphenyl-1,3-bis((*R*)-1-phenylethyl)-imidazolidine **5** was prepared from (1*S*,2*S*)-1,2-diphenyl-*N*,*N*′-bis((*R*)-1-phenylethyl)ethane-1,2-diamine (1.00 g, 2.39 mmol), 2-chlorobenzaldehyde (336 mg, 2.39 mmol) and *p*-toluenesulfonic acid (50 mg) in benzene (75 mL) according to method A. The reaction mixture was refluxed for 48 h. FCC gave the *title compound* (−)-**5** as a white solid (640 mg, 50%). Mp 57–58 °C; $[\alpha]_D^{22} = -99.9$ (*c* 1.6, $CHCl_3$) MS (ESI, 0 V), *m*/*e* 541.2 (M^+-H, 100%); IR (KBr) 3027m, 1492s, 1453vs, 1222s, 1133s, 1027s, 756vs, 700vs cm^{-1}; ^1H NMR (400 MHz): δ 8.02 (d, $J = 7.7$ Hz, 1H), 7.40–6.70 (m, 23H), 6.00 (s, 1H, NC*H*N), 4.38 (d, $J = 8$ Hz, 1H, NC*H*Ph), 4.10 (d, $J = 8$ Hz, 1H, NC*H*Ph), 3.92–3.89 (m, 1H, C*H*CH_3), 3.70–3.67 (m, 1H, C*H*CH_3), 1.16 (d, $J = 8.1$ Hz, 3H, CHC*H*$_3$), 0.78 (d, $J = 7.0$ Hz, 3H, CHC*H*$_3$); ^{13}C NMR (100 MHz): δ 145.5, 142.7, 142.4, 140.6, 140.5, 134.8, 132.3, 129.2, 128.5, 128.4, 128.3, 128.1, 127.8, 127.75, 127.73, 127.67, 127.2, 127.0, 126.97, 126.93, 126.3, 126.0, 76.2 (N*C*HN), 74.7 (*C*HPh), 72.4 (*C*HPh), 58.6 (CH*C*H_3), 56.5 (CH*C*H_3), 21.7 (CH*C*H_3), 20.1 (CH*C*H_3). Anal. Calcd for $C_{37}H_{35}ClN_2$: C, 81.82; H, 6.50; 6.53; N, 5.16. Found: C, 81.78; H, 6.91; N, 5.05.

4.2.9. (−)-(4*S*,5*S*)-2-(4-Chlorophenyl)-4,5-diphenyl-1,3-bis((*R*)-1-phenylethyl)imidazolidine 6. (−)-(4*S*,5*S*)-2-(4-Chlorophenyl)-4,5-diphenyl-1,3-bis((*R*)-1-phenylethyl)imidazolidine **6** was prepared from (1*S*,2*S*)-1,2-diphenyl-*N*,*N*′-bis((*R*)-1-phenylethyl)ethane-1,2-diamine (821 mg, 2.00 mmol) and 4-chlorobenzaldehyde (290 mg, 2.00 mmol) according to method B. FCC gave the *title compound* (−)-**6** as a white solid (833 mg, 77%). Mp 53 °C; $[\alpha]_D^{22} = -12.8$ (*c* 0.2, $CHCl_3$); MS (ESI, 0 V), *m*/*e* 541.3 (M^+−H, 10%); IR (KBr) 3026m, 1490s, 1452s, 1225m, 1088m, 832m, 765s, 700vs cm^{-1}; ^1H NMR (200 MHz): δ 7.30–6.80 (m, 24H), 5.11 (s, 1H, NC*H*N), 4.31 (d, $J = 8.3$ Hz, 1H, NC*H*Ph), 4.14 (d, $J = 8.3$ Hz, 1H, NC*H*Ph), 3.90 (q, $J = 7.0$ Hz, 1H, C*H*CH_3), 3.44 (q, $J = 7.0$ Hz, 1H, C*H*CH_3), 0.99 (d, $J = 7.0$ Hz, 3H, CHC*H*$_3$), 0.67 (d, $J = 7.0$ Hz, 3H, CHC*H*$_3$); ^{13}C NMR (50 MHz): δ 145.6, 143.4, 143.3, 141.5, 140.9, 132.5, 130.9, 128.3, 128.25, 128.1, 128.0, 127.9, 127.8, 127.6, 127.3, 127.13, 127.06, 126.9, 126.6, 126.2, 81.6 (N*C*HN), 75.8 (*C*HPh), 73.2 (*C*HPh), 60.4 (CH*C*H_3), 58.3 (CH*C*H_3), 24.7 (CH*C*H_3), 21.6 (CH*C*H_3). HRMS calculated for $C_{37}H_{36}ClN_2^+$: 543.2562; found: 543.2563.

4.2.10. (−)-(4*S*,5*S*)-1,3-Dimethyl-2-(2-((4*S*,5*S*)-1,3-dimethyl-4,5-diphenylimidazolidin-2-yl)phenyl)-4,5-diphenylimidazolidine 7. (−)-(4*S*,5*S*)-1,3-Dimethyl-2-(2-((4*S*,5*S*)-1,3-dimethyl-4,5-diphenylimidazolidin-2-yl)phenyl)-4,5-diphenylimidazolidine **7** was prepared from (1*S*,2*S*)-*N*,*N*′-dimethyl-1,2-diphenylethane-1,2-diamine (960 mg, 4 mmol) and phthaldialdehyde (269 mg, 2 mmol) according to method B as a yellow solid (1.01 g, 87%). Mp 83–85 °C; $[\alpha]_D^{22} = -89.8$ (*c* 0.44, $CHCl_3$); MS (EI), *m*/*e* 578 (M^+, 1%), 368 (100), 180 (20), 142 (10), 118 (20), 91 (10), 77 (10), 52 (10); IR (KBr) 3452vs, 1631m, 1451m, 1264m, 1161m, 1103m, 755s, 699s cm^{-1}; ^1H NMR (400 MHz): δ 8.13–8.11 (m, 2H), 7.57–7.50 (m, 2H), 7.48–7.27 (m, 20H), 5.52 (s, 2H, NC*H*N), 3.92 (d, $J = 8.4$ Hz, 2H, C*H*Ph), 3.59 (s, 2H, C*H*Ph), 2.18 (s, 6H, NCH_3), 2.07 (s, 6H, NCH_3); ^{13}C NMR (100 MHz): δ 141.8, 140.3, 138.9, 129.6, 128.9, 128.8, 128.5, 128.4, 128.3, 128.0, 127.6, 83.7 (N*C*HN), 78.8 (*C*HPh), 38.9 (N*C*H_3), 38.0 (N*C*H_3); HRMS calculated for $C_{40}H_{43}N_4^+$: 579.3488; found: 579.3466.

4.2.11. (+)-(3a*R*,7a*R*)-Octahydro-2-(2-((3a*R*,7a*R*)-octahydro-1,3-dimethyl-1*H*-benzo[*d*]imidazol-2-yl)phenyl)-1,3-dimethyl-1*H*-benzo[*d*]imidazole 8. (+)-(3a*R*,7a*R*)-Octahydro-2-(2-((3a*R*,7a*R*)-octahydro-1,3-dimethyl-1*H*-benzo[*d*]-imidazol-2-yl)phenyl)-1,3-dimethyl-1*H*-benzo[*d*]imidazole **8** was prepared from (1*R*,2*R*)-*N*,*N*′-dimethylcyclohexane-1,2-diamine (119 mg, 0.84 mmol) and phthaldialdehyde (56 mg, 0.42 mmol) according to method B as a yellow solid (159 mg, 99%). Mp 98 °C; $[\alpha]_D^{22} = +103.6$ (*c* 1.48, $CHCl_3$); MS (ESI, 0 V), *m*/*e* 383.3 (M^++H, 100%); IR (KBr) 3441s, 2972s, 2931vs, 2455s, 2791s, 1452s, 1360s, 1190s, 1009s, 758s cm^{-1}; ^1H NMR (200 MHz): δ 7.80–7.60 (m, 2H), 7.32–7.27 (m, 2H), 4.85 (s, 2H, NC*H*N), 2.18 (s, 6H, NCH_3), 1.93 (s, 6H, NCH_3) 2.50–2.00 (m, 4H, NC*H*CH_2), 2.10–1.80 (m, 8H), 1.40–1.10 (m, 8H); ^{13}C NMR (50 MHz): δ 139.0,, 129.1, 127.4, 84.0 (N*C*HN), 69.8 (N*C*HCH_2), 68.98 (N*C*HCH_2), 37.3 (N*C*H_3), 37.0 (N*C*H_3), 29.4 (*C*H_2), 29.0 (*C*H_2), 24.7 (C*C*H_2), 24.4 (*C*H_2). HRMS calculated for $C_{24}H_{39}N_4^+$: 383.3169; found: 383.3171.

4.3. Preparation of salts

4.3.1. General procedure for the preparation of imidazolinium bromide salts. Imidazolidine (1 mmol) was dissolved in a minimal amount of 1,2-dimethoxyethane. *N*-Bromoacetamide (1 mmol) was added in two portions (0.5 mmol each) in an interval of 15 min. After the addition of the second portion, the reaction mixture was stirred for an additional hour. Diethyl ether (5 mL) was added and an oily solid formed. The solvent was decanted and the remaining solid was washed with diethyl ether (3 mL) and dried under high vacuum to give the corresponding bromide salt.

4.3.2. General procedure for the counter anion exchange with potassium hexafluorophosphate, lithium bis(trifluoromethylsulfonyl)imide or sodium tetrakis(3,5-bis(trifluoromethyl)-phenyl)borate. Imidazolinium bromide salt (1 mmol) was dissolved in $CHCl_3$ (3 mL) and stirred vigorously with 1 equiv of KPF_6, $LiNTf_2$ or $NaB[3,5\text{-}(CF_3)_2\text{-}C_6H_3]_4$ in water (3 mL) for 30 min. The organic phase was separated, washed with water (3 × 3 mL) and dried over molecular sieves 3 Å. The solvent was evaporated and the product further dried overnight under high vacuum to give the corresponding imidazolinium hexafluorophosphate, bis-(trifluoromethylsulfonyl)imide or tetrakis(3,5-bis(trifluoromethyl)phenyl)borate salt.

4.3.3. (−)-(4*S*,5*S*)-2-(2-Chlorophenyl)-1,3-dimethyl-4,5-diphenylimidazolinium hexafluorophosphate *ent*-1b. (−)-(4*S*,5*S*)-2-(2-Chlorophenyl)-1,3-dimethyl-4,5-diphenylimidazolinium hexafluorophosphate *ent*-**1b** was prepared from (−)-(4*S*,5*S*)-2-(2-chlorophenyl)-1,3-dimethyl-4,5-diphenylimidazolidine *ent*-**1** (200 mg, 0.55 mmol) and NBA (80 mg, 0.55 mmol) in glyme (2 mL), followed by a counter anion exchange with KPF_6 (103 mg, 0.55 mmol) in a mixture of DCM (3 mL) and water (3 mL) as a white solid (245 mg, 88%). Mp 277 °C; $[\alpha]_D^{22} = -116.7$ (*c* 0.36, $CHCl_3$); MS (ESI, 0 V), *m*/*e* 361.1 (M^+, 100%); IR (KBr) 3453s, 1608vs, 837vs, 754s, 702s, 557s cm^{-1}; ^1H NMR (200 MHz): δ 8.20–8.10 (m, 1H), 7.56–7.32 (m, 13H), 5.42 (d, $J = 12.2$ Hz, 1H, C*H*), 5.00 (d, $J = 12.2$ Hz, 1H, C*H*Ph) 2.87 (s, 3H, NCH_3), 2.78 (s, 3H, NCH_3); ^{13}C NMR (50 MHz): δ 164.3 (N*C*$^+$N), 134.5, 134.3, 132.7, 131.6, 131.0, 130.4, 130.3, 130.2, 129.9, 129.8, 129.2, 128.5, 127.9, 121.5, 75.8 (*C*HPh), 74.4 (*C*HPh), 32.8 (N*C*H_3), 32.6 (N*C*H_3). HRMS (ESI) calculated for $C_{23}H_{22}N_2Cl^+$: 361.1472, found: 361.1458.

4.3.4. (+)-(4*R*,5*R*)-2-(2-Chlorophenyl)-1,3-dimethyl-4,5-diphenylimidazolinium bis(trifluoromethylsulfonyl)imide 1c. (+)-(4*R*,5*R*)-2-(2-Chlorophenyl)-1,3-dimethyl-4,5-diphenylimidazolinium bis(trifluoromethylsulfonyl)imide **1c** was prepared from aminal **1** (61 mg, 0.169 mmol) and NBA (24.5 mg, 0.17 mmol) in glyme (1 mL), followed by a counter anion exchange with $LiNTf_2$ (50 mg 97%, 0.17 mmol) in a mixture of $CHCl_3$ (3 mL) and water (3 mL) as a colourless oil (63 mg, 58%). $[\alpha]_D^{22} = +86.5$ (*c* 0.28, $CHCl_3$); MS (ESI, 0 V), *m*/*e* 361.0 (M^+, 100%); IR (KBr) 1607s, 1352s, 1195vs, 1135s, 1058s, 760m, 653m cm^{-1}; ^1H NMR

(400 MHz): δ 8.18–8.12 (m, 1H), 7.75–7.65 (m, 3H), 7.55–7.45 (m, 8H), 7.40–7.32 (m, 2H), 5.43 (d, $J = 12.1$ Hz, 1H, C*H*Ph), 4.99 (d, $J = 11.8$ Hz, 1H, C*H*Ph), 2.88 (s, 3H, NCH_3), 2.80 (s, 3H, NCH_3); ^{13}C NMR (100 MHz): δ 164.9 (NC$^+$N), 135.1, 134.7, 133.1, 131.9, 131.8, 131.0, 130.7, 130.65, 130.4, 130.3, 129.8, 128.8, 128.3, 121.9, 121.88, 76.5 (*C*HPh), 75.1 (*C*HPh), 33.6 (NH*C*H$_3$), 33.1 (NH*C*H$_3$). HRMS (ESI) calculated for $C_{23}H_{22}N_2Cl^+$: 361.1472, found: 361.1458.

4.3.5. (−)-(4*S*,5*S*)-2-(4-Chlorophenyl)-1,3-dimethyl-4,5-diphenylimidazolinium bromide 2a. (−)-(4*S*,5*S*)-2-(4-Chlorophenyl)-1,3-dimethyl-4,5-diphenylimidazolinium bromide **2a** was prepared from (4*S*,5*S*)-2-(4-chlorophenyl)-1,3-dimethyl-4,5-diphenylimidazolidine **2** (359 mg, 0.99 mmol) and NBA (144 mg, 0.99 mmol) in glyme (3 mL) as a white solid (446 mg, 99%). *Hygroscopic*. Mp 98 °C; $[\alpha]_D^{22} = -56.5$ (*c* 0.35, $CHCl_3$); MS (ESI, 0 V), *m*/*z* 361 (M^+, 100%); IR (KBr) 1605s, 1345s, 1327s, 1199vs, 1138s, 1058s, 616s cm^{-1}; ^{1}H NMR (200 MHz): δ 8.08 (d, $J = 8.34$ Hz, 2H), 7.58–7.55 (m, 6H), 7.38–7.35 9 (m, 6H), 5.33 (s, 2H, C*H*Ph), 2.87 (s, 6H, CH_3); ^{13}C NMR (50 MHz$_3$): δ 166.6 (NC$^+$N), 139.9, 133.4, 130.43, 130.38, 130.1, 129.7, 128.3, 120.3, 75.2 (*C*HPh), 33.6 (NCH_3); HRMS (ESI) calculated for $C_{23}H_{22}N_2Cl^+$: 361.1472, found: 361.1482.

4.3.6. (−)-(4*S*,5*S*)-2-(4-Chlorophenyl)-1,3-dimethyl-4,5-diphenylimidazolinium bis(trifluoromethylsulfonyl)imide 2c. (−)-(4*S*,5*S*)-2-(4-Chlorophenyl)-1,3-dimethyl-4,5-diphenylimidazolinium bis(trifluoromethylsulfonyl)imide **2c** was prepared from (4*S*,5*S*)-2-(4-chlorophenyl)-1,3-dimethyl-4,5-diphenylimidazoliumbromide **2a** (330 mg, 0.75 mmol) and $LiNTf_2$ (236 mg, 0.82 mmol) in a mixture of $CHCl_3$ (2 mL) and water (2 mL) as a white solid (347 mg, 82%). Mp 102 °C; $[\alpha]_D^{22} = -62.4$ (*c* 0.34, $CHCl_3$); MS (EI), *m*/*e* 360 (M^+−H, 100%), 327 (5), 283 (5), 152 (10), 78 (5), 69 (30); IR (KBr) 1604vs, 1346vs, 1199vs, 1138s, 1158s, 616s, 512s cm^{-1}; ^{1}H NMR (200 MHz): δ 7.70–7.59 (m, 4H), 7.43–7.31 (m, 10H), 5.05 (s, 2H, C*H*Ph), 4.64 (s, 6H, NCH_3); ^{13}C NMR (50 MHz): δ 166.6 (NC$^+$N), 140.2, 133.3, 130.5, 130.3, 130.2, 129.8, 128.1, 120.0, 75.2 (*C*HPh), 33.6 (NCH_3). HRMS (ESI) calculated for $C_{23}H_{22}N_2Cl^+$: 361.1472, found: 361.1470.

4.3.7. (−)-(4*S*,5*S*)-2-(4-Chlorophenyl)-1,3-dimethyl-4,5-diphenylimidazolinium tetrakis(3,5-bis(trifluoromethyl)phenyl)borate 2d. (−)-(4*S*,5*S*)-2-(4-Chlorophenyl)-1,3-dimethyl-4,5-diphenylimidazolinium tetrakis(3,5-bis(trifluoromethyl)-phenyl)borate **2d** was prepared from (4*S*,5*S*)-2-(4-chlorophenyl)-1,3-dimethyl-4,5-diphenylimidazolinium bromide **2a** (150 mg, 0.34 mmol) and NaB[3,5-$(CF_3)_2$-C_6H_3]$_4$ (300 mg, 0.34 mmol) in a mixture of $CHCl_3$ (3 mL) and water (3 mL) as a white solid (48 mg, 71%). mp 114 °C; $[\alpha]_D^{22} = -39.4$ (*c* 0.31, $CHCl_3$); MS (EI), *m*/*e* 361 (M^+, 20%), 243 (100), 228 (20), 165 (20), 152 (20), 118 (25); IR (KBr) 3426m, 1604s, 1356vs, 1278vs, 1127vs, 839s, 713s, 682s, 669m cm^{-1}; ^{1}H NMR (400 MHz): δ 7.80–7.69 (m, 10H), 7.59–7.46 (m, 12H), 7.26–7.25 (m, 4H), 4.98 (s, 2H, C*H*), 2.92 (s, 6H, CH_3); ^{13}C NMR (50 MHz) 166.4 (NC$^+$N), 162.1 (q, $J = 49.6$ Hz, B*C*), 142.3, 135.2 (BC*C*H), 133.8, 131.7, 131.5, 130.9, 129.5, 129.3 (q, $J = 28.4$ Hz, *C*CF$_3$), 126.9, 126.3, 125.0 (q, $J = 271$ Hz, C*C*F$_3$), 118.9, 117.95 (*C*HCCF$_3$), 75.5 (N*C*HPh), 34.2 (N*C*H$_3$). Anal. Calcd for $C_{55}H_{34}BClF_{24}$: C, 53.92; H, 2.80; N, 2.29. Found: C, 53.72; H, 2.84; N, 2.20; HRMS (ESI) calculated for $C_{23}H_{22}N_2Cl^+$: 361.1472, found: 361.1483.

4.3.8. (−)-(4*S*,5*S*)-2-(2-Pyridinyl)-4,5-diphenyl-1,3-bis((*R*)-1-phenylethyl)imidazolinium bromide 4a. (−)-(4*S*,5*S*)-2-(2-Pyridinyl)-4,5-diphenyl-1,3-bis((*R*)-1-phenylethyl)imidazolinium bromide **4a** was prepared from (4*S*,5*S*)-2-(pyridinyl)-4,5-diphenyl-1,3-bis((*R*)-1-phenylethyl)imidazolidine **4** (1.13 g, 2.23 mmol) and NBA (308 mg, 2.23 mmol) in Et_2O (5 mL) as a yellow oil (1.26 g, 96%). *Hygroscopic*. $[\alpha]_D^{22} = -85.9$ (*c* 0.67, $CHCl_3$); ^{1}H NMR (200 MHz): δ 9.57 (d, $J = 7.7$ Hz, 1H), 8.90 (d, $J = 3.8$ Hz, 1H), 8.32 (t, $J = 7.7$ Hz, 1H), 7.80–7.70 (8m, 1H), 7.30–6.90 (m, 20H), 5.20–4.90 (m, 4H, NC*H*Ph, PhC*H*CH$_3$), 1.65 (br s, 6H, CHCH_3); ^{13}C NMR (50 MHz): δ 164.2 (NC$^+$N), 150.3, 143.1, 139.4, 136.4, 135.1, 129.3, 129.2, 128.4, 128.3, 127.9, 127.6, 127.4, 72.1 (*C*HPh), 57.8 (N*C*HCH$_3$), 18.1 (CH*C*H$_3$); HRMS (ESI) calculated for $C_{36}H_{34}N_3^+$: 508.2753, found: 508.2758.

4.3.9. (−)-(4*S*,5*S*)-2-(2-Pyridinyl)-4,5-diphenyl-1,3-bis((*R*)-1-phenylethyl)imidazolinium hexafluorophosphate 4b. (−)-(4*S*,5*S*)-2-(2-Pyridinyl)-4,5-diphenyl-1,3-bis((*R*)-1-phenylethyl)imidazolinium hexafluorophosphate **4b** was prepared from (4*S*,5*S*)-2-(2-pyridyl)-4,5-diphenyl-1,3-bis((*R*)-1-phenylethyl)imidazolinium bromide **4a** (105 mg, 0.18 mmol) and KPF_6 (36 mg, 0.20 mmol) in a mixture of $CHCl_3$ (3 mL) and water (3 mL) as a white solid (100 mg, 86%). Mp 87 °C; $[\alpha]_D^{22} = -65.4$ (*c* 0.48, $CHCl_3$); MS (ESI, 0 V), *m*/*e* 508 (M^+); IR (KBr) 3423w, 1556s, 1456m, 1278m, 838vs, 757m, 696s, 557s cm^{-1}; ^{1}H NMR (200 MHz): δ 9.00 (d, $J = 4.2$ Hz, 1H) 8.58 (d, $J = 7.8$ Hz, 1H), 8.34–8.30 (m, 1H), 7.79–7.73 (m, 1H), 7.26–6.99 (m, 20H), 5.00–4.80 (m, 4H, C*H*Ph, C*H*CH$_3$), 1.56 (d, $J = 6.8$ Hz, 6H, NCH_3); ^{13}C NMR (50 MHz): δ 164.1 (NC$^+$N), 151.4, 142.7, 139.4, 136.0, 135.2, 129.5, 129.4, 128.7, 128.5, 127.9, 127.7, 126.6, 126.4, 71.4 (*C*HPh), 57.8 (N*C*HCH$_3$), 17.9 (CH*C*H$_3$); HRMS (ESI) calculated for $C_{36}H_{34}N_3^+$: 508.2753, found: 508.2752.

4.3.10. (−)-(4*S*,5*S*)-2-(2-Pyridinyl)-4,5-diphenyl-1,3-bis((*R*)-1-phenylethyl)imidazolinium bis(trifluoromethylsulfonyl)-imide 4c. (−)-(4*S*,5*S*)-2-(2-Pyridinyl)-4,5-diphenyl-1,3-bis((*R*)-1-phenylethyl)imidazolinium bis(trifluoromethylsulfonyl)imide **4c** was prepared from (4*S*,5*S*)-2-(2-pyridyl)-4,5-diphenyl-1,3-bis((*R*)-1-phenylethyl)imidazolinium bromide **4a** (300 mg, 0.51 mmol) and $LiNTf_2$ (176 mg, 0.61 mmol) in a mixture of DCM (3 mL) and water (3 mL) as a colourless liquid (230 mg, 57%). $[\alpha]_D^{22} = -50.0$ (*c* 0.46, $CHCl_3$); MS (ESI, 0 V), *m*/*e* 508.3 (M^+); IR (KBr) 1556m, 1353s, 1196vs, 1135m, 1058s, 696m cm^{-1}; ^{1}H NMR (200 MHz): δ 8.95–8.87 (m, 1H) 8.50 (d, $J = 6.8$ Hz, 1H), 8.27 (td, $J = 7.7$, 1.7 Hz, 1H), 7.75–7.60 (m, 1H), 7.25–6.70 (m, 20H), 4.90–4.70 (m, 4H, C*H*Ph, C*H*CH$_3$), 1.50 (d, $J = 7.0$ Hz, 6H, NCH_3); ^{13}C NMR (50 MHz): δ 163.1 (NC$^+$N), 150.1, 141.7, 138.5, 135.1, 134.2, 129.9, 128.4, 127.8, 127.5, 126.9, 126.7, 125.6, 125.4, 119.0 (q, $J = 64.9$ Hz, *C*F$_3$), 70.5 (*C*HPh), 56.8

(N*C*HCH$_3$), 12.0 (CH*C*H$_3$). HRMS (ESI) calculated for $C_{36}H_{34}N_3^+$: 508.2753, found: 508.2767.

4.3.11. (−)-(4*S*,5*S*)-2-(2-Chlorophenyl)-4,5-diphenyl-1,3-bis((*R*)-1-phenylethyl)imidazolinium bromide 5a. (−)-(4*S*,5*S*)-2-(2-Chlorophenyl)-4,5-diphenyl-1,3-bis((*R*)-1-phenylethyl)imidazolinium bromide **5a** was prepared from (4*S*,5*S*)-2-(2-chlorophenyl)-4,5-diphenyl-1,3-bis((*R*)-1-phenylethyl)imidazolidine **5** (100 mg, 0.18 mmol) and NBA (26.8 mg, 0.18 mmol) in glyme (1 mL) as a white solid (102 mg, 89%). *Hygroscopic*. $[\alpha]_D^{22} = -131.6$ (*c* 0.29, $CHCl_3$); ^{1}H NMR (400 MHz): δ 9.41 (d, $J = 7.2$, 1H), 7.90 (t, $J = 7.2$ Hz, 1H), 7.70 (t, $J = 7$ Hz, 1H), 7.55–6.90 (m, 18H), 6.65–6.58 (m, 2H), 6.63 (d, $J = 10.3$ Hz, 1H, C*H*Ph), 5.34 (q, $J = 7.2$ Hz, 1H, C*H*CH$_3$), 5.08 (d, $J = 10.3$ Hz, 1H, C*H*Ph), 4.83 (q, $J = 7.2$ Hz, 1H, C*H*CH$_3$), 1.75 (d, $J = 7.1$ Hz, 6H, CHC*H*$_3$); ^{13}C NMR (100 MHz): δ 165.3 (N*C*$^+$N), 138.03, 138.0, 136.0, 134.7, 134.2, 137.7, 132.8, 130.6, 129.95, 129.87, 129.7, 129.6, 129.5, 128.9, 128.7, 128.6, 128.5, 128.4, 128.2, 127.7, 123.5, 73.4 (*C*HPh), 72.9 (*C*HPh), 60.7 (N*C*HCH$_3$), 57.2 (N*C*HCH$_3$), 19.8 (CH*C*H$_3$), 17.0 (CH*C*H$_3$). This compound was used directly in the subsequent step.

4.3.12. (−)-(4*S*,5*S*)-2-(2-Chlorophenyl)-4,5-diphenyl-1,3-bis((*R*)-1-phenylethyl)imidazolinium hexafluorophosphate 5b. (−)-(4*S*,5*S*)-2-(2-Chlorophenyl)-4,5-diphenyl-1,3-bis((*R*)-1-phenylethyl)imidazolinium hexafluorophosphate **5b** was prepared from (4*R*,5*R*)-2-(2-chlorophenyl)-4,5-diphenyl-1,3-bis((*S*)-1-phenylethyl)imidazolinium bromide **5a** (88 mg, 0.14 mmol) and KPF_6 (29 mg, 0.16 mmol) in a mixture of $CHCl_3$ (3 mL) and water (3 mL) as a white solid (92 mg, 94%). Mp = 160 °C; $[\alpha]_D^{22} = -82.7$ (*c* 2.75, $CHCl_3$); MS (ESI, 0 V), *m*/*e* 541.3 (M^+, 100%); IR (Kbr) 2360m, 2341m, 1533s, 1456m, 840vs, 697s, 558s cm^{-1}; ^{1}H NMR (400 MHz): δ 8.49 (dd, $J = 7.7$, 1.4 Hz, 1H), 8.01–7.95 (m, 1H), 7.78 (td, $J = 5.6$, 1.5 Hz, 1H), 7.64 (d, $J = 8.0$ Hz, 1H), 7.40–6.95 (m, 16H), 6.85–6.80 (m, 2H), 6.65 (d, $J = 7.4$ Hz, 2H), 5.19 (d, $J = 8.4$ Hz, 1H, C*H*Ph), 5.00 (d, $J = 8.4$ Hz, 1H, C*H*Ph), 4.98 (q, $J = 7.1$ Hz, 1H, C*H*CH$_3$), 4.88 (q, $J = 7.1$ Hz, 1H, C*H*CH$_3$), 1.74 (d, $J = 7.1$ Hz, 3H, CHC*H*$_3$), 1.68 (d, $J = 7.1$ Hz, 3H, CHC*H*$_3$); ^{13}C NMR (100 MHz): δ 164.9 (N*C*$^+$N), 137.8, 136.6, 135.5, 135.2, 132.5, 132.4, 131.1, 130.5, 130.0, 129.9, 129.87, 129.8, 128.9, 128.7, 128.3, 127.8, 127.7, 127.65, 123.0, 72.6 (*C*HPh), 72.6 (*C*HPh), 59.8 (N*C*HCH$_3$), 57.7 (N*C*HCH$_3$), 18.4 (CH*C*H$_3$), 17.6 (CH*C*H$_3$); HRMS (ESI) calculated for $C_{37}H_{24}N_2Cl^+$: 541.2421, found: 541.2421.

4.3.13. (+)-(4*S*,5*S*)-2-(4-Chlorophenyl)-4,5-diphenyl-1,3-bis((*R*)-1-phenylethyl)imidazolinium hexafluorophosphate 6b. (+)-(4*S*,5*S*)-2-(4-Chlorophenyl)-4,5-diphenyl-1,3-bis((*R*)-1-phenylethyl)imidazolinium hexafluorophosphate **6b** was prepared when (4*S*,5*S*)-2-(4-chlorophenyl)-4,5-diphenyl-1,3-bis((*R*)-1-phenylethyl)imidazolidine **6** (200 mg, 0.368 mmol) was dissolved in glyme (1 mL) and NBA (27 mg, 0.18 mmol) added. The reaction mixture was stirred at rt for 15 min and a second portion of NBA (27 mg, 0.18 mmol) added. The reaction mixture was stirred for an additional 30 min, during which a yellow solid precipitated. Et_2O (3 mL) was added and the mixture stirred for 15 min in order to precipitate the rest of the imidazolinium bromide salt. The solvent was removed by filtration and the remaining solid washed with Et_2O (2 × 3 mL). The solid was dissolved in $CHCl_3$ (3 mL) and an aqueous solution of KPF_6 (68 mg, 0.368 mmol) was added. The mixture was stirred vigorously for 30 min and the aqueous phase removed. The organic phase was washed with water (3 × 3 mL), dried (3 Å MS) and the solvent was removed under reduced pressure to give the *title compound* **6b** as a yellow solid (183 mg, 72%). Mp 87 °C; $[\alpha]_D^{22} = +5.7$ (*c* 0.39, $CHCl_3$); MS (ESI, 0 V), *m*/*e* 541.0 (M^+, 100%); IR (KBr) 3441s, 1543m, 848vs, 696s, 557s cm^{-1}; ^{1}H NMR (200 MHz): δ 7.85 (dd, $J = 27.8$, 8.6 Hz, 4H), 7.40–6.75 (m, 20H), 4.97 (s, 2H, NC*H*Ph), 5.00–4.85 (m, 2H, NC*H*Me), 1.60 (d, $J = 7.2$ Hz, 6H, CHC*H*$_3$); ^{13}C NMR (50 MHz): δ 166.7 (N*C*$^+$N), 140.1, 136.1, 135.5, 131.0, 130.2, 129.6, 129.5, 128.7, 128.6, 126.6, 120.9, 71.7 (2C, N*C*HPh), 58.0 (2C, N*C*HCH$_3$), 17.9 (2C, CH*C*H$_3$); HRMS (ESI) calculated for $C_{37}H_{34}N_2Cl$: 541.2411, found: 541.2418.

4.3.14. (−)-(4*S*,5*S*)-1,3-Dimethyl-2-(2-((4*S*,5*S*)-1,3-dimethyl-4,5-diphenylimidazolidin-2-yl)phenyl)-4,5-diphenylimidazolinium bis-bis(trifluoromethylsulfonyl)imide 7c. (4*S*,5*S*)-1,3-Dimethyl-2-(2-((4*S*,5*S*)-1,3-dimethyl-4,5-diphenylimidazolidin-2-yl)phenyl)-4,5-diphenylimidazolidine **7** (500 mg, 0.864 mmol) was dissolved in glyme (3 mL) and NBA (128 mg, 0.864 mmol) was added. After 15 min, a second portion of NBA (128 mg, 0.864 mmol) was added. The reaction mixture was stirred overnight and Et_2O (5 mL) was added in order to precipitate the bromide salt formed. The precipitate was washed with Et_2O (2 × 5 mL) and dried in vacuo for 30 min. The bromide salt was dissolved in $CHCl_3$ (3 mL) and a solution of $LiNTf_2$ (574.16 mg, 2 mmol) in H_2O (2 mL) added. The mixture was stirred vigorously for 30 min, during which a white precipitate formed. The latter was filtered off, washed with $CHCl_3$ (3 mL), water (3 mL) and dried in vacuo to give the *title compound* **7c** as a white solid (622 mg, 80%). Mp 165 °C; $[\alpha]_D^{22} = -21$ (*c* 0.2, acetone); MS (ESI, 0 V), *m*/*e* 288 (M^{2+}, 100%), 856 (M^++NTf_2, 20); IR (KBr) 3425m, 1602s, 1350vs, 1197vs, 1058s, 616s cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.40–8.20 (m, 4H), 7.80–7.30 (m, 20H), 5.82 (d, $J = 14.0$ Hz, 2H, C*H*Ph), 5.39 (d, $J = 14.0$ Hz, 2H, C*H*Ph), 3.00–2.80 (m, 12H, NC*H*$_3$); ^{13}C NMR (100 MHz, DMSO-d_6): δ 164.9 (N*C*$^+$N), 135.5, 134.6, 132.0, 133.2, 131.2, 130.8, 130.4, 130.2, 129.9, 129.85, 121.9, 120.4 (q, $J = 314.3$ Hz, CF_3), 76.4 (*C*HPh), 72.0 (*C*HPh), 35.4 (N*C*H$_3$), 34.9 (N*C*H$_3$). HRMS (ESI) calculated for $C_{40}H_{40}N_4^{2+}$: 288.1626, found: 288.1621.

4.3.15. (−)-(4*S*,5*S*)-1,3-Dimethyl-2-(2-((4*S*,5*S*)-1,3-dimethyl-4,5-diphenylimidazolidin-2-yl)phenyl)-4,5-diphenylimidazolinium bis-tetrakis(3,5-bis(trifluoromethyl)phenyl)borate 7d. (4*S*,5*S*)-1,3-Dimethyl-2-(2-((4*S*,5*S*)-1,3-dimethyl-4,5-diphenylimidazolidin-2-yl)phenyl)-4,5-diphenylimidazolidine **7** (250 mg, 0.43 mmol) was dissolved in a minimal amount of glyme (2 mL) and NBA (62 mg, 0.43 mmol) was added. After 15 min stirring at rt, a second portion of NBA (62 mg, 0.43 mmol) was added. The reaction mixture was stirred overnight and Et_2O (5 mL) was added in order to precipitate the formed bromide salt. The precipitate was washed with Et_2O (2 × 5 mL) and dried in vacuo for

30 min. The bromide salt was then dissolved in DCM (5 mL), followed by the addition of NaB[3,5-$(CF_3)_2$-$C_6H_3]_4$ (765.8 mg, 0.86 mmol) and water (3 mL). The mixture was stirred vigorously for 30 min. The organic phase was separated, washed with water (3 × 5 mL), dried (3 Å MS) and the solvent removed under reduced pressure. The remaining solid was further dried under high vacuum to give the *title compound* **7d** as a light brown solid (792 mg, 80%). Mp 66–68 °C; $[\alpha]_D^{22} = -25$ (*c* 0.45, acetone); MS (ESI, 0 V), *m/e* 288.2 (M^{2+}, 100%); IR (KBr) 1605m, 1356s, 1279vs, 1126s, 682m cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 8.30–8.20 (m, 4H), 7.60–7.40 (m, 44H), 5.91 (d, $J = 14.0$ Hz, 2H, C*H*Ph), 5.47 (d, $J = 14.0$ Hz, 2H, C*H*Ph), 2.99 (d, $J = 5.1$ Hz, 12H, NCH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 164.5 (NC^+N), 161.5 (q, $J = 49.6$ Hz, B*C*), 135.1, 134.2 (b, B*C*CH), 134.4, 133.6, 132.8, 130.7, 130.3, 130.0, 129.7, 129.5, 129.4, 128.9 (q, $J = 28.4$ Hz, CH*C*CF_3), 124.4 (q, $J = 271.2$ Hz, C*C*F_3), 121.6, 118.0 (*C*HCCF_3), 79.6 (N*C*HPh), 71.6 (N*C*HPh), 35.0 (N*C*H_3), 34.5 (N*C*H_3). HRMS (ESI) calculated for $C_{20}H_{20}N_2^{2+}$ 288.1626, found 288.1616.

4.3.16. (−)-(4*R*,5*R*)-1,3-Dimethyl-2-(2-((4*R*,5*R*)-1,3-dimethyl-4,5-diphenylimidazolidin-2-yl)phenyl)-4,5-diphenylimidazolinium bis-hexafluorophosphate 8b. (3a*R*,7a*R*)-Octahydro-2-(2-((3a*R*,7a*R*)-octahydro-1,3-dimethyl-1*H*-benzo[*d*]imidazol-2-yl)phenyl)-1,3-dimethyl-1*H*- benzo[*d*]-imidazole **8** (140 mg, 0.37 mmol) was dissolved in a minimal amount of glyme (1.5 mL) and NBA (53 mg, 0.37 mmol) was added. After 15 min stirring at rt, a second portion (53 mg, 0.37 mmol) was added. The reaction mixture was stirred for 3 h during which a brown precipitate formed. The solvent was decanted and the precipitate washed with Et_2O and dissolved in $CHCl_3$ (2 mL). A solution of KPF_6 (135 mg, 0.732 mmol) in water (3 mL) was added and the mixture was vigorously stirred overnight during which a brown precipitate formed. The solvents were carefully removed and the rest was dried in vacuo to give the *title compound* **8b** as a brown solid (184 mg, 75%). Mp 145–150 °C; $[\alpha]_D^{22} = -7.7$ (*c* 0.3, acetone); MS (ESI, 50 V), *m/e* 190.1 (M^{2+}, 100%); IR (KBr) 2360m, 1589m, 839vs, 558s cm^{-1}; ^1H NMR (400 MHz, DMSO): δ 8.20–8.10 (m, 2H), 8.10–7.95 (m, 2H), 3.65–3.50 (m, 4H, C*H*), 3.05 (s, 6H, CH_3), 2.85 (s, 6H, CH_3), 2.40–2.25 (m, 4H, CH_2), 2.00–1.85 (m, 4H, CH_2), 1.60–1.25 (m, 8H, CH_2); ^{13}C NMR (100 MHz, DMSO): δ 165.3 (NC^+N), 134.5, 131.8, 121.8, 69.2 (N*C*HCH_2), 67.6 (N*C*HCH_2), 33.7 (*C*H_3), 32.8 (*C*H_3), 27.4 (*C*H_2), 27.3 (*C*H_2), 23.9 (*C*H_2), 23.7 (*C*H_2). HRMS (ESI) calculated for $C_{24}H_{36}N_4^{2+}$ 190.1471, found: 190.1470.

4.3.17. (−)-(4*R*,5*R*)-1,3-Dimethyl-2-(2-((4*R*,5*R*)-1,3-dimethyl-4,5-diphenylimidazolidin-2-yl)phenyl)-4,5-diphenylimidazolinium bis-tetrakis(3,5-bis(trifluoromethyl)phenyl)-borate 8d. (3a*R*,7a*R*)-Octahydro-2-(2-((3a*R*,7a*R*)-octahydro-1,3-dimethyl-1*H*-benzo[*d*]imidazol-2-yl)phenyl)-1,3-dimethyl-1*H*-benzo[*d*]imidazole **8** (145 mg, 0.38 mmol) was dissolved in a minimal amount of glyme (3 mL) and NBA (55 mg, 0.19 mmol) was added. After 15 min stirring at rt a second portion (55 mg, 0.19 mmol) was added and the reaction mixture stirred for 3 h. Et_2O (5 mL) was added in order to precipitate the bromide salt formed. The precipitate was washed with Et_2O (2 × 5 mL) and dried in vacuo for 30 min. The bromide salt was dissolved in DCM (3 mL) and NaB[3,5-$(CF_3)_2$-$C_6H_3]_4$ (672.5 mg, 0.759 mmol) and water (3 mL) were added. The mixture was vigorously stirred for 30 min and the organic phase separated, washed with water (3 × 5 mL), dried (3 Å MS) and the solvent removed under reduced pressure. The remaining solid was further dried under high vacuum to give the *title compound* **8d** as a brown solid (677 mg, 87%). Mp 115 °C; $[\alpha]_D^{22} = -5.9$ (*c* 0.67, acetone); MS (ESI, 20 V), *m/e* 190.1 (M^{2+}, 100%); IR (KBr) 1612w, 1357s, 1280vs, 1125vs, 713m cm^{-1}; ^1H NMR (400 MHz, DMSO): δ 8.10–7.95 (m, 4H), 7.70–7.50 (m, 24H), 3.60–3.50 (m, 4H, NC*H*CH_2), 3.01 (s, 6H, NCH_3), 2.83 (s, 6H, CH_3), 2.40–2.20 (m, 4H, CH_2), 1.90–1.80 (m, 4H, CH_2), 1.60–1.40 (m, 4H, CH_2), 1.40–1.20 (m, 4H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.9 (NC^+N), 160.0 (q, $J = 49.6$ Hz, B*C*), 134.0, 131.3, 128.4 (q, $J = 62.4$ Hz, *C*CF_3), 123.9 (q, $J = 271$ Hz, C*C*F_3), 121.2, 117.3, 68.7 (N*C*HCH_2), 67.1 (N*C*HCH_2), 33.1 (*C*H_3), 32.2 (*C*H_3), 26.7 (*C*H_2), 23.2 (*C*H_2), 23.0 (*C*H_2). HRMS (ESI) calculated for $C_{24}H_{36}N_4^{2+}$ 190.1470, found: 190.1469.

4.4. Imidazolinium salts as catalysts

4.4.1. General procedure for the imidazolinium salt catalyzed aza Diels–Alder reaction in acetonitrile. An imine (0.2 mmol) and catalyst (0.02 mmol, 10 mol %) were placed into a dry Schlenk flask under a nitrogen atmosphere. The reaction mixture was dissolved in dry acetonitrile (2 mL) and Danishefsky's diene (0.22 mmol, 43 μL) was added at once. After 16 h stirring at rt, the mixture was quenched with a saturated solution of potassium hydrogencarbonate (2 mL) and extracted with ethyl acetate (3 × 5 mL). The organic phases were combined, dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. FCC (petroleum ether/ethyl acetate, 1/1) gave the desired product.

4.4.2. General procedure for the imidazolinium salt catalyzed inverse electron demand aza Diels–Alder reaction for mono-imidazolinium salts. Imine **10** (0.2 mmol) and the catalyst (0.02 mmol) were placed into a dry Schlenk flask under a nitrogen atmosphere. The reaction mixture was dissolved in dry acetonitrile (2 mL) and the dienophile 3,4-dihydro-2*H*-pyran **12** (0.4 mmol, 30.27 μL) or 3,4-dihydro-2*H*-pyran **13** (0.4 mmol, 36.18 μL) was added at once. The reaction mixture was stirred at rt between 16 and 112 h and the solvent was evaporated under reduced pressure. The products were isolated by FCC (petroleum ether/ethyl acetate, 95/5) to give the corresponding quinolines.

4.4.3. In DCM, catalyzed by bis-imidazolinium salts. *N*-Benzylidene aniline (54.3 mg, 0.3 mmol) and the catalyst (0.03 mmol) were placed into a dry Schlenk flask under a nitrogen atmosphere. The reaction mixture was dissolved in dry DCM (1 mL) and 3,4-dihydro-2*H*-pyran (56 μL, 0.6 mmol) added at once. The reaction mixture was stirred at rt (for different reaction times and temperatures see text in Section 2.2). The solvent was removed and the crude product purified by FCC (petroleum ether/ethyl acetate, 95/5) to give the corresponding quinolines.

4.4.4. 2,3-Dihydro-1,2-diphenylpyridin-4(1*H*)-one 11 (R = Ph). 2,3-Dihydro-1,2-diphenylpyridin-4(1*H*)-one **11** was prepared from **9** and **10** (R = Ph) as yellow solid. The spectral data were consistent with the literature values.[25]

4.4.5. 2-Phenyl-1-tosyl-2,3-dihydropyridin-4(1*H*)-one 11 (R = Ts). From (E)-N-(benzylidene) tosylamine (52 mg, 0.20 mmol) and Danishefsky's diene (43 μL, 0.22 mmol) in the presence of imidazolinium catalyst (0.02 mmol) as a white solid (23 mg, 35%). Spectral data were consistent with literature values.[26]

4.4.6. 3,4,4a,5,6,10b-Hexahydro-5-phenyl-2*H*-pyrano[3,2-*c*]-quinoline 14a and 14b. 3,4,4a,5,6,10b-Hexahydro-5-phenyl-2*H*-pyrano[3,2-*c*]quinoline **14a** and **14b** was prepared from benzylidene aniline (54 mg, 0.3 mmol) and dihydropyran (50 μL, 0.6 mmol) as a mixture of *cis*- and *trans*-diastereomers. The ratio of the diastereomers was determined after isolation by FCC.

Cis-isomer as a white solid: The spectral data were consistent with the literature values.[27] HPLC conditions: AD-H (2.5% *i*-PrOH/hexane, 0.3 mL/min) $t_1 = 71.2$ min, $t_2 = 83.8$ min.

Trans-isomer as a yellow oil: The spectral data were consistent with the literature values.[27] HPLC conditions: AD-H (2.5% *i*-PrOH/hexane, 0.4 mL/min) $t_1 = 38.5$ min, $t_2 = 59.1$ min.

4.5. NMR experiments with Mosher's acid salt

4.5.1. Preparation of racemic potassium Mosher's carboxylate. Racemic Mosher's acid (302 mg, 1.29 mmol) was dissolved in water (1 mL) and a solution of KOH (72 mg, 1.29 mmol) in water (3 mL) was added. The mixture was stirred at rt for 15 min and water was removed under reduced pressure. The remaining solid was further dried under high vacuum to give the potassium Mosher's carboxylate salt as a white solid (351 mg, quant.).

4.5.2. NMR experiment with the racemic Mosher's acid salt. Mosher's acid salt (1 mmol) and the corresponding imidazolinium salt (1 mmol) were dissolved in acetone-d_6 and the ^{1}H NMR and ^{19}F NMR spectra were recorded at rt. For results see Table 4.

Acknowledgements

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Unexpected behaviour of tosylated and acetylated imidazolinium salts

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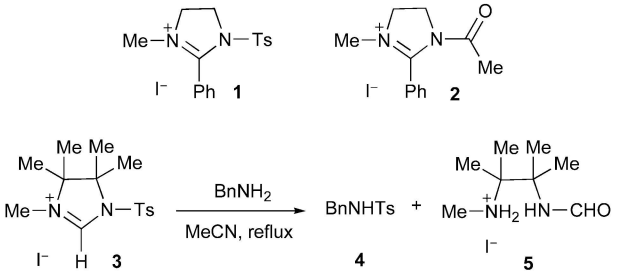
Tosylated and acetylated imidazolinium salts revealed an unexpected reactivity when treated with methyl iodide or benzyl bromide. Moreover an unprecedented acid-catalysed rearrangement for an acetylated imidazolinium salt was observed during an anion metathesis.

Introduction

Tetrahydrofolate coenzymes, which are part of a one-carbon fragment biochemical transfer,[1,2] can be mimicked by several simple imidazolinium salts.[3,4] For example, the imidazolinium iodide salt analogues **1**, **2** and **3** (Scheme 1) were first prepared from the corresponding imidazolines and MeI by Pandit's group.[5]



Scheme 1

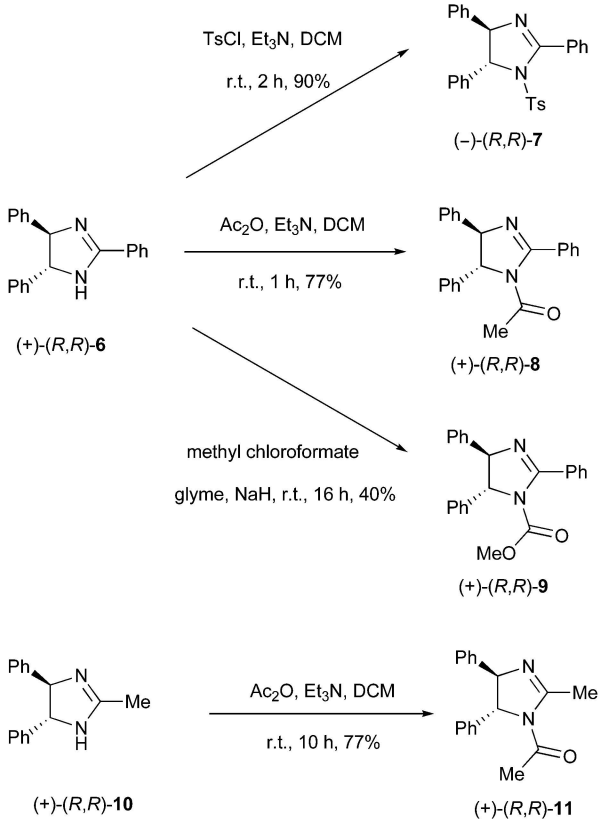
The much hindered tosylated analogue **3** revealed a different behaviour than less hindered salts. When heated with an amine, *e.g.* benzylamine, the tosyl group was attacked by the nucleophile and the imidazoline ring left the molecule and was isolated as the hydrolytic product **5**.[5] This observation is very rare for imidazolinium analogues, however very well known for tosylated imidazolium salts, like 1-(toluenesulfonyl)-3-methylimidazolium triflate, which has been used as a tosylating reagent for alcohols[6] and amines.[7,8] The resulting imidazol ring in this reaction is not hydrolysed.

Moreover, a few chiral imidazolinium salts have recently been reported as chiral ionic liquids.[9,10] However, the examples of this emerging class of chiral ionic liquids remain few compared to other types of chiral ionic liquids.[11,12] In addition it is possible to apply 2-phenyl substituted imidazolinium salts as ionic liquids with strong bases.[13]

Recently, we have reported the application of some achiral imidazolinium salts as catalysts for the aza Diels–Alder reaction.[14] The salts may be considered as part of the limited number of metal-free Lewis acids[15–21] and could contribute to the important research field of organocatalysis.[22,23] In order to apply chiral analogues of the salts as catalysts, we were interested in preparing chiral analogues of **1** and **2**, since the electron withdrawing groups could increase the catalytic activity of these salts. Here we would like to discuss some unexpected results along the synthetic route towards some of the desired chiral tosyl and acetyl substituted imidazolinium salts, which, to the best of our knowledge, have not been reported so far.

Results and discussion

First the precursors for the desired salts were prepared. Therefore, (+)-(*R*,*R*)-**6**,[24] prepared from (+)-(*R*,*R*)-1,2-diphenyl-1,2-ethylenediamine,[25] was treated with tosyl chloride or acetic acid anhydride in the presence of triethylamine to give the imidazoline derivatives (−)-(*R*,*R*)-**7** and (+)-(*R*,*R*)-**8** in 90 and 77% yield, respectively (Scheme 2). In addition imidazoline (+)-(*R*,*R*)-**9** was synthesised in 40% yield, by the reaction of methyl chloroformate with (+)-(*R*,*R*)-**6** in the presence of sodium hydride (Scheme 2).



Scheme 2

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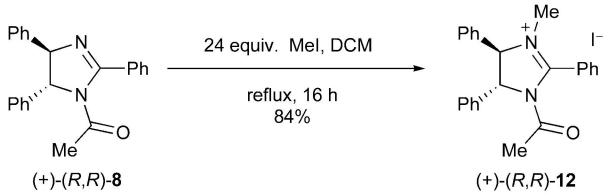
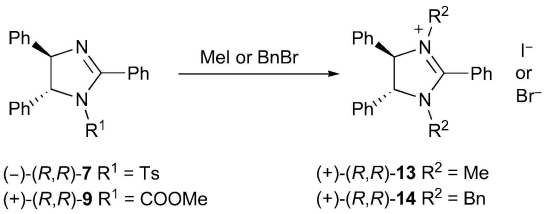
Moreover, imidazoline (+)-(*R*,*R*)-**11** was obtained *via* an acetylation of (+)-(*R*,*R*)-**10**,[26] derived from (+)-(*R*,*R*)-1,2-diphenyl-1,2-ethylenediamine,[25] in 77% yield (Scheme 2).

In order to transform imidazoline **8** into the desired salt **12** the method reported for salts **1** and **2** was applied.[5] An excess of methyl iodide was refluxed with **3** in dichloromethane for 16 h. Therefore (+)-(4*R*,5*R*)-1-acetyl-2,4,5-triphenyl-*trans*-4,5-dihydroimidazole (**8**) yielded (+)-(4*R*,5*R*)-1-acetyl-2,4,5-triphenyl-3-methyl-*trans*-imidazolinium iodide (**12**) in 84% (Scheme 3).



Scheme 3

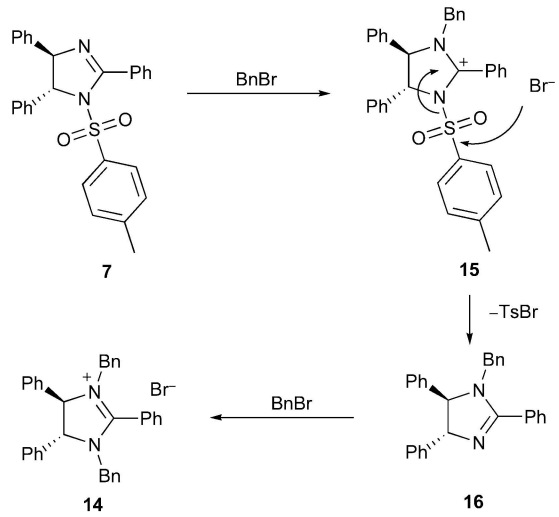
Additionally, imidazolines **7** and **9** were treated the same way. However, in both cases not the expected salts were found as the major products. Instead the dimethylated salt **13** was observed (Scheme 4). In the crude NMR mainly the dimethylated product **13** was detected besides the starting material and the desired product. The latter could be isolated neither *via* column chromatography nor by recrystallisation. When the reaction was performed in dichloromethane at 85 °C in a sealed vessel, only **13** was obtained from **7** and **9** in quantitative yield. The replacement of methyl iodide with dimethyl sulfate resulted in both cases in a complex mixture of compounds. When **11** was treated with methyl iodide only a complex mixture of compounds was found.



Scheme 4

After these unexpected results 3 equiv. of benzyl bromide was used in the reaction with **7** and **9**, respectively (Scheme 4). A reaction in refluxing dichloromethane was not observed. When the reaction was performed at 85 °C in a sealed tube, mainly the dibenzylated product **14** was found next to some starting material. In acetonitrile a total conversion to **14** took place. The bromide salt **14** was isolated in a yield of 74% after recrystallisation. A repeat of the reaction in acetonitrile and 1 equiv. of benzyl bromide resulted in the isolation of the starting material and **14** in a ratio of 1 : 1 by NMR.

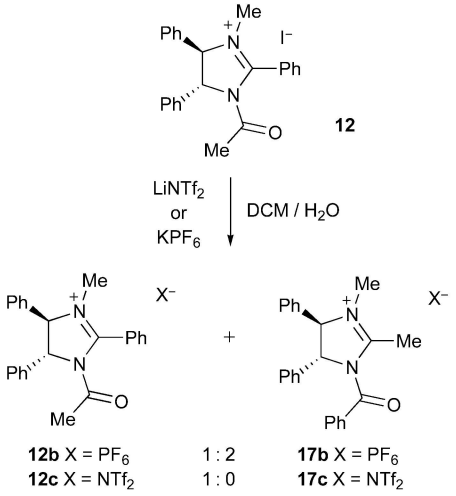
These results may be explained by the following proposed mechanism (Scheme 5), taking the behaviour of salt **3** (Scheme 1) into consideration. In the first step the desired product, *e.g.* **15** is formed. Taking the nucleophilicity of halide anions in polar aprotic solvents into account, the bromide anion of salt **15** can attack at the sulfonyl group in a bimolecular substitution reaction. The formation of tosyl bromide is assisted by the generation of the very good leaving group, the imidazole **16**. In the last step **16** can



Scheme 5

react with another benzyl bromide molecule to the dibenzylated product **14**. The starting material **7** reacts with benzyl bromide far slower then **16**, due to the electron withdrawing tosyl group, which explains, that even when just 1 equiv. of benzyl bromide was used **14** and **7** were observed. When the reaction was repeated with 0.9 equiv. of benzyl bromide and stopped after 6 h, it was possible to isolate **16** in 5% yield through column chromatography. For the reactions involving **9** and methyl iodide a similar mechanism could be assumed.

In order to transform salt **12** into analogues with different anions, **12** was stirred in the presence of 1.5 equiv. of KPF_6 or $LiNTf_2$ in a mixture of dichloromethane and water. The organic phase was separated and washed three times with water. The more lipophilic ion pair remains in the organic solvent. In the case of $LiNTf_2$ the expected salt **12c** was isolated in pure form in 90% yield (Scheme 6). However, the corresponding PF_6^- salt was isolated in only 48% yield. The result of the simple anion exchange was quite amazing. In the NMR spectra all aliphatic signals were twice as much as required and it was found that the unexpected product (+)-(4*R*,5*R*)-1-benzoyl-2,3-dimethyl-4,5-diphenyl-*trans*-imidazolinium hexafluorophosphate (**17b**) was



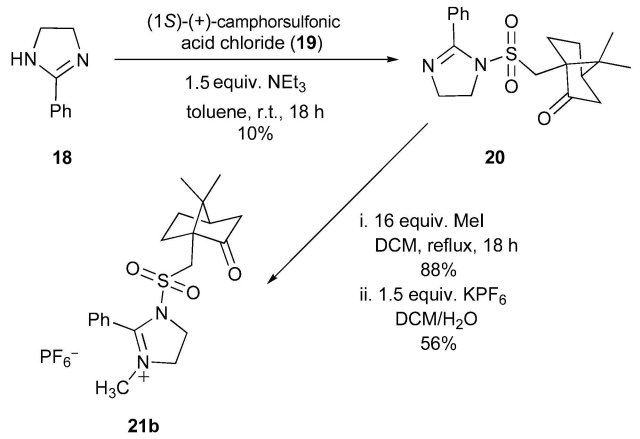
Scheme 6

present. The ratio of the two products was calculated according to the ^{1}H NMR spectra with **12b** : **17b** = 1 : 2.

After the discovery of the unexpected rearrangement product **17b**, further experiments were carried out to find mechanistic clues to describe the reaction in detail. A possible reason for the result may be due to the use of KPF_6. Considering that potassium hexafluorophosphate contains traces of HF and can slowly decompose further in water, a catalytic amount of acid was used to influence the 1 : 2 ratio of the mixture **12b** : **17b**. Manipulation of the mixture **12b** : **17b** = 1 : 2 with a catalytic amount of aqueous HCl in dichloromethane shifted the equilibrium to **12b** : **17b** = 1 : 3. The reduced solubility of HCl in dichloromethane could explain the poor movement of the ratio. Therefore, the next reaction was carried out with a solution of trifluoroacetic acid in dichloromethane. Now the generation of the rearrangement product **12b** : **17b** was more favoured and appeared according to ^{1}H NMR spectra in a ratio of 1 : 6 after 24 h. No total conversion of **12b** to **17b** was obtained, probably an equilibrium exists, wherein an excess of **17b** is thermodynamically favoured. In view of the empiric support, that the rearrangement is catalysed by acidic conditions, a last procedure was tested. (+)-(4*R*,5*R*)-1-Acetyl-2,4,5-triphenyl-3-methyl-*trans*-imidazolinium trifluoromethanesulfonimide **12c** was stirred with a catalytic amount of trifluoroacetic acid in dichloromethane. The expected mixture of **12c** : **17c** occurred in a ratio of 1 : 4 after 24 h.

Two possible mechanisms are imaginable: first a rearrangement *via* non-ring opening. After the formation of an enol a four membered ring could be formed followed by a 1,3-phenyl shift. Advantages of this proposed mechanism are no ring openings, permanently just one charge in the molecule, which can be stabilised by tautomerism, and the necessity of a catalytic amount of acid to form an enol in the first step. On the other hand, there is also a disadvantage: constitution of the positively charged [3.2.0]-system in the transition state. The second possible mechanism would be a ring opening of the cation, followed by the formation of the new salt with the former carbonyl carbon atom at the C-2 position.

Finally, in order to explore the behaviour of an aliphatic sulfone rest group, (1*S*)-(+)-camphorsulfonyl-(2-phenyl-4,5-dihydro)-imidazole (**20**) was prepared in a low yield (Scheme 7) from 2-phenyl-4,5-dihydroimidazole (**18**)[5] and (1*S*)-(+)-camphorsulfonic acid chloride (**19**) under basic conditions. The imidazoline **20** was then treated with methyl iodide and after an anion exchange the expected product **21b** was isolated. No side reactions were observed (Scheme 7).



Scheme 7

In conclusion, we have reported some unexpected behaviour of tosylated and acetylated imidazolinium salts, which may be important to consider for the preparation of new imidazolinium based ionic liquids and tetrahydrofolate coenzyme model compounds.

Experimental

General experimental

All reactions were conducted under a protective atmosphere of dry nitrogen. Dichloromethane and acetonitrile were distilled from calcium hydride. All other chemicals, whose preparation is not described below, were bought from Aldrich, Fluka, Merck or Lancaster and were used without further purification. 2-Phenyl-4,5-dihydroimidazole (**18**),[5] (+)-(4*R*,5*R*)-2,4,5-triphenyl-*trans*-4,5-dihydro-1*H*-imidazole[24] (**6**) and (+)-(4*S*,5*S*)-2-methyl-4,5-diphenyl-*trans*-4,5-dihydro-1*H*-imidazole[26] (**10**) were prepared according to literature procedures. Reactions were monitored by TLC with Merck Silica gel 60 F_{254} plates or with neutral aluminium oxide 60 F_{254} plates. Flash column chromatography[27] was performed on Sorbisil C-60 or active neutral aluminium oxide 90. Infrared spectra were recorded on a Vector 22 FT-IR from Bruker. NMR spectra were performed in $CDCl_3$ at ambient temperature on a Bruker AMX 400 and a Bruker AC 200F. The following symbols are used to analyse the ^{13}C-spectra: +: primary or tertiary carbon, −: secondary carbon, q: quaternary carbon. Mass spectra were recorded on MS 5889 B from Hewlett Packard. Electron spray mass spectrometry was performed directly on a MS LC/MSD 1100 MSD from Hewlett Packard. High resolution mass spectra were recorded by Dr Dräger at the Institute of Organic Chemistry, University of Hanover. Elemental analyses were carried out by the Institute of Pharmaceutical Chemistry, Technical University of Braunschweig and are reported as the average of two runs. Optical rotations were measured on a Perkin-Elmer 243 B polarimeter. Melting points were taken with an apparatus after Dr Tottoli and are uncorrected.

(+)-(4*R*,5*R*)-1-(Toluene-4-sulfonyl)-2,4,5-triphenyl-*trans*-4,5-dihydroimidazole (7). (+)-(4*R*,5*R*)-2,4,5-Triphenyl-*trans*-4,5-dihydro-1*H*-imidazole (**6**) (2.5 g, 8.4 mmol) and triethylamine (1.15 mL, 8.4 mmol) were dissolved in dry dichloromethane (20 mL). After adding tosyl chloride (1.76 g, 9.2 mmol) the resulting mixture was stirred for 2 h at r.t. The precipitate was filtered off and the filtrate was washed with dilute sodium bicarbonate solution and dried (Na_2SO_4). Evaporation yielded a thick oil, which was purified by column chromatography on silica with petroleum ether–ethyl acetate (5 : 1) as the eluent to give the title compound **7** as a white solid (3.4 g, 7.5 mmol, 90%). $[\alpha]_D^{24}$ = −150 (c = 1.02, CH_2Cl_2), mp 122 °C; MS (EI), m/e 453 (M + 1, 10%), 297 (70), 91 (100); IR (KBr) 3443w, 1634s, 1368s, 1175s, 761s cm^{-1}; ^{1}H NMR (200 MHz) δ 7.87–7.82 (m, 2 H, Ar–H), 7.56–7.40 (m, 8 H, Ar–H), 7.25–7.05 (m, 7 H, Ar–H), 6.83–6.78 (m, 2 H, Ar–H), 5.10 (s, 2 H, C–H), 2.40 (s, 3 H, Me); ^{13}C NMR (50 MHz) δ 159.9 (q, N*C*N), 144.7 (q, Ar), 142.5 (q, Ar), 141.8 (q, Ar), 134.9 (q, Ar), 131.4 (+, Ar), 130.5 (q, Ar), 130.0 (+, Ar), 129.7 (Ar), 129.3 (+, Ar), 128.7 (+, Ar), 128.3 (+, Ar), 128.0 (+, Ar), 127.9 (+, Ar), 127.4 (+, Ar), 126.2 (+, Ar), 126.0 (+, Ar),

77.4 (+, C(5)–H), 72.6 (+, C(4)–H), 21.7 (+, Me). Anal. calcd for $C_{27}H_{24}O_2N_2S_1$: C, 73.61; H, 5.49; N, 6.36. Found: C, 73.87; H, 5.32; N, 6.33%.

(+)-(4*R*,5*R*)-1-Acetyl-2,4,5-triphenyl-*trans*-4,5-dihydroimidazole (8). (+)-(4*R*,5*R*)-2,4,5-Triphenyl-*trans*-4,5-dihydro-1*H*-imidazole (**6**) (1.0 g, 3.36 mmol) was dissolved in dry dichloromethane (12 mL). Acetic anhydride (0.32 mL, 3.36 mmol) and triethylamine (0.32 mL, 3.36 mmol), dissolved in dichloromethane (2 mL), were added to the mixture and left to stir for 1 h at r.t. The mixture was washed with water and dried (Na_2SO_4). After evaporation of the solvent, the crude product was purified by column chromatography on Al_2O_3 using petroleum ether–ethyl acetate (4 : 1) as the eluent to give the title compound **8** as a colourless oil (0.88 g, 2.6 mmol, 77%). $[a]_D^{24} = 42$ ($c = 1.12$ in CH_2Cl_2); MS (EI), *m/e* 340 (*M*, 5%), 193 (100), 91 (40); IR (KBr) 3445m, 3029m, 1696s, 1622m, 1321s, 1273m, 1024m, 760s, 697s cm^{-1}; ^1H NMR (200 MHz) δ 7.81–7.76 (m, 2 H, Ar–H), 7.52–7.28 (m, 13 H, Ar–H), 5.19 (dd, $J = 3.2$ Hz, $J = 11.5$ Hz, 2 H, C–H), 1.89 (s, 3 H, Me); ^{13}C NMR (50 MHz) δ 168.6 (q, C=O), 160.1 (q, N*C*N), 141.9 (q, Ar), 141.2 (q, Ar), 131.9 (q, Ar), 130.8 (+, Ar), 129.4 (+, Ar), 129.1 (+, Ar), 128.4 (+, Ar), 128.2 (+, Ar), 128.0 (+, Ar), 126.1 (+, Ar), 125.5 (+, Ar), 77.1 (+, C(5)–H), 70.6 (+, C(4)–H), 25.0 (+, Me). HRMS (ESI) found: $M + H$ 341.1658. $C_{23}H_{21}N_2O$ requires: 341.1654.

(+)-(4*R*,5*R*)-2,4,5-Triphenyl-*trans*-4,5-dihydroimidazole-1-carboxylic acid methyl ester (9). A sodium hydride solution (60% in petroleum) (0.17 g, 4.4 mmol) was washed with glyme (3 × 5 mL) and then additional glyme (20 mL) was added. A glyme solution (15 mL) of (+)-(4*R*,5*R*)-2,4,5-triphenyl-*trans*-4,5-dihydro-1*H*-imidazole (**6**) (1 g, 3.36 mmol) was slowly added and the mixture was stirred for 2 h. Methyl chloroformate (0.34 mL, 4.36 mmol) was then added quickly. The mixture was stirred at r.t. for 19 h, filtered and the filtrate was evaporated in vacuum. Purification by column chromatography on Al_2O_3 using petroleum ether–ethyl acetate (5 : 1) as the eluent afforded the title compound **4** as a colourless oil (0.48 g, 1.3 mmol, 40%). $[a]_D^{24} = 63$ ($c = 1.03$ in $CHCl_3$); MS (EI), *m/e* 356 (*M*, 50%), 193 (100); IR (KBr) 2962s, 1735m, 1331m, 1262s, 1101s, 1022s, 801s cm^{-1}; ^1H NMR (200 MHz) δ 7.83–7.78 (m, 2 H, Ar–H), 7.53–7.29 (m, 13 H, Ar–H), 5.18 (d, $J = 4.3$ Hz, 1 H, C–H), 5.16 (d, $J = 4.3$ Hz, 1 H, C–H) 3.55 (s, 3 H, Me); ^{13}C NMR (50 MHz) δ 160.1 (q, C=O), 152.8 (q, N*C*N), 142.6 (q, Ar), 141.8 (q, Ar), 131.5 (q, Ar), 130.7 (+, Ar), 129.3 (+, Ar), 129.1 (+, Ar), 128.8 (+, Ar), 128.2 (+, Ar), 128.0 (+, Ar), 126.3 (+, Ar), 125.8 (+, Ar), 77.5 (+, C(5)–H), 70.6 (+, C(4)–H), 53.3 (+, Me). HRMS(ESI) found: $M + H$ 357.1611. $C_{23}H_{21}N_2O$ requires: 357.1603.

(+)-(4*S*,5*S*)-1-Acetyl-2-methyl-4,5-diphenyl-*trans*-4,5-dihydroimidazole (11). (+)-(4*S*,5*S*)-2-Methyl-4,5-diphenyl-*trans*-4,5-dihydro-1*H*-imidazole (**10**) (2 g, 8.5 mmol) was dissolved in absolute ethanol (15 mL). Acetic anhydride (0.8 mL, 8.5 mmol) and triethylamine (1.2 mL, 8.5 mmol) dissolved in dichloromethane (2 mL) were added to the mixture, after which the resulting solution was stirred for 10 h at r.t. After evaporation of the solvent the residue was purified by column chromatography on Al_2O_3 using petroleum ether–ethyl acetate (3 : 1) as the eluent to give the crude product as a yellow solid. Recrystallisation in ethanol gave the title compound **11** as a white solid (1.8 g, 6.5 mmol, 77%). $[a]_D^{24} = 136$ ($c = 1.14$ in CH_2Cl_2), mp 133 °C; MS (EI), *m/e* 278 (*M*, 10%), 236 (10), 148 (30), 131 (100), 106 (70), 89 (60); IR (KBr) 1684s, 1641m, 1379s, 1332s, 760s, 700s cm^{-1}; ^1H NMR (200 MHz) δ 7.47–7.31 (m, 6 H, Ar–H), 7.23–7.17 (m, 4 H, Ar–H), 4.86 (dd, $J = 1.9$ Hz, $J = 5.1$ Hz, 2 H, C–H), 2.69 (d, $J = 1.1$ Hz, 3 H, N=C–Me), 1.88 (s, 3 H, CO–Me); ^{13}C NMR (50 MHz) δ 169.1 (q, C=O), 159.5 (q, N*C*N), 141.93 (q, Ar), 141.91 (q, Ar), 129.6 (+, Ar), 129.0 (+, Ar), 128.3 (+, Ar), 127.9 (+, Ar), 126.1 (+, Ar), 125.2 (+, Ar), 77.8 (+, C(5)–H), 70.7 (+, C(4)–H), 25.0 (+, N=C–*Me*), 19.3 (+, CO*Me*). Anal. calcd for $C_{18}H_{18}O_1N_2$: C, 77.67; H, 6.52; N, 10.06. Found: C, 77.50; H, 6.57; N, 10.11%.

(+)-(4*R*,5*R*)-1-Acetyl-2,4,5-triphenyl-3-methyl-*trans*-imidazolinium iodide (12). Compound **8** (1 g, 2.9 mmol) was dissolved in dry dichloromethane (22 mL). Methyl iodide (2.2 mL) was added and the mixture was refluxed. After 1 h another portion of methyl iodide (2.2 mL) was added and the mixture was refluxed overnight. Evaporation yielded the desired product **12** as a yellowish solid (1.2 g, 2.5 mmol, 84%). $[a]_D^{24} = 66$ ($c = 0.51$ in CH_3CN), mp 155 °C; ESI, *m/e* 355 (M^+, 100%); IR (KBr) 3048s, 3015s, 1747s, 1622s, 1497s, 1449s, 1427s, 1276s, 1225s, 756s, 701s cm^{-1}; ^1H NMR (200 MHz) δ 7.71–7.31 (m, 15 H, Ar–H), 6.01 (d, $J = 11.4$ Hz, 1 H, C–H), 5.79 (d, $J = 11.4$ Hz, 1 H, C–H), 3.03 (s, 3 H, N–Me), 1.86 (s, 3 H, CO–Me); ^{13}C NMR (50 MHz) δ 168.7 (q, C=O), 166.27 (q, N*C*N), 135.5 (q, Ar), 133.3 (+, Ar), 132.1 (q, Ar), 130.6 (+, Ar), 129.9 (+, Ar), 129.7 (+, Ar), 129.53 (+, Ar), 129.47 (+, Ar), 128.2 (+, Ar), 123.5 (q, C^+), 75.8 (+, C(5)–H), 71.7 (+, C(4)–H), 35.1 (+, N–*Me*), 26.4 (+, CO*Me*). HRMS (ESI) found: M^+ 355.1826. $C_{24}H_{23}N_2O$ requires: 355.1810.

(+)-(4*R*,5*R*)-1-Acetyl-2,4,5-triphenyl-3-methyl-*trans*-imidazolinium trifluoromethanesulfonimide (12c). Salt **12** (0.2 g, 0.41 mmol) was dissolved in dry dichloromethane (5 mL). 2 equiv. (0.24 g, 0.83 mmol) of *N*-lithiotrifluoromethanesulfonimide were added and the mixture was stirred for 2 h at room temperature. After adding water (5 mL) and additional stirring for 1 h, the phases were separated and the organic layer was washed three times with water, dried (Na_2SO_4) and evaporated under vacuum. Drying on the vacuum line at 40 °C (oil bath temperature) yielded the title compound **12c** as a yellowish solid (238 mg, 0.4 mmol, 90%). $[a]_D^{24} = 115$ ($c = 0.35$ in CH_2Cl_2), mp 50–51 °C; ESI, *m/e* 355 (M^+, 100%); IR (KBr) 3068w, 2360s, 2342s, 1744s, 1624s, 1502m, 1458m, 1352s, 1195s, 1132m, 1057m cm^{-1}; ^1H NMR (200 MHz) δ 7.72–7.68 (m, 3 H, Ar–H), 7.53–7.36 (m, 12 H, Ar–H), 5.69 (d, $J = 9.7$ Hz, 1 H, C–H), 5.28 (d, $J = 9.6$ Hz, 1 H, C–H), 2.95 (s, 3 H, N–Me), 1.80 (s, 3 H, CO–Me); ^{13}C NMR (50 MHz) δ 168.1 (q, C=O), 166.5 (q, N*C*N), 136.2 (q, Ar), 133.7 (+, Ar), 132.6 (q, Ar), 130.9 (+, Ar), 129.9 (+, Ar), 129.8 (+, Ar), 129.4 (+, Ar), 129.2 (+, Ar), 128.3 (+, Ar), 123.1 (q, Ar), 120.2 (q, $J = 65.0$ Hz, CF_3), 75.9 (+, C(5)–H), 71.0 (+, C(4)–H), 34.3 (+, N–*Me*), 25.3 (+, CO*Me*); HRMS(ESI) found: M^+ 355.1820. $C_{24}H_{23}N_2O$ requires: 355.1810.

(+)-(4*R*,5*R*)-1-Acetyl-2,4,5-triphenyl-3-methyl-*trans*-imidazolinium hexafluorophosphate (12b) and (+)-(4*R*,5*R*)-1-benzoyl-2,3-methyl-4,5-diphenyl-*trans*-imidazolinium hexafluorophosphate (17b). Salt **12** (0.2 g, 0.41 mmol) was dissolved in dry dichloromethane (5 mL). 1.5 equiv. potassium hexafluorophosphate (0.11 g, 0.62 mmol) were added and the mixture was

stirred for 24 h at room temperature. After adding water (5 mL) the stirring was continued for another hour. The phases were separated by using a pipette and the organic layer was washed with water (2 × 2 mL), dried (Na_2SO_4) and evaporated under reduced pressure. Crystallisation in methanol yielded white crystals (88 mg, 0.2 mmol, 48%). The ratio (**17b** : **12b** = 2 : 1) was determined by ^{1}H NMR. Enrichment of **12b** could be obtained after two recrystallisations in diethyl ether–hexane (**17b** : **12b** = 1 : 4). ^{1}H NMR (200 MHz) δ 7.76–7.21 (m, 22.5 H, Ar–H of **12b** + **17b**), 5.73 (d, J = 10.0 Hz, 0.5 H, C–H of **12b**), 5.60 (d, J = 11.6 Hz, 1 H, C–H of **17b**), 5.34 (d, J = 10.0 Hz, 0.5 H, C–H of **12b**), 5.23 (d, J = 11.4 Hz, 1 H, C–H of **17b**), 3.14 (s, 3 H, N–Me of **17b**), 2.96 (s, 1.5 H, N–Me of **12b**), 2.46 (s, 3 H, C$^+$–Me of **17b**), 1.80 (s, 1.5 H, CO–Me of **12b**). ^{13}C NMR (50 MHz) δ 168.1 (q, C=O, **12b** + **17b**), 168.0 (q, N*C*N, **17b**), 166.5 (q, N*C*N, **12b**), 136.2 (q, Ar, **12b**), 134.5 (q, Ar, **17b**), 134.1 (q, Ar, **17b**), 133.7 (+, Ar, **12b**), 132.6 (q, Ar, **12b**), 132.5 (+, Ar, **17b**), 131.0 (+, Ar, **12b**), 130.7 (q, Ar, **17b**), 130.0 (+, Ar, **17b**), 129.9 (+, Ar, **12b**), 129.7 (+, Ar, **12b**), 129.5 (+, Ar, **17b**), 129.3 (+, Ar, **12b**), 129.2 (+, Ar, **12b** + **17b**), 128.5 (+, Ar, **12b** + **17b**), 127.8 (+, Ar, **17b**), 123.1 (q, Ar, **17b**), 122.9 (q, Ar, **12b**), 75.8 (+, C(5)–H, **12b**), 75.2 (+, C(5)–H, **17b**), 72.3 (+, C(4)–H, **17b**), 71.0 (+, C(4)–H, **12b**), 34.3 (+, N–*Me*, **12b**), 33.3 (+, N–*Me*, **17b**), 25.3 (+, CO*Me*, **12b**), 16.0 (+, C*Me*, **17b**).

(+)-(4*R*,5*R*)-1,3-Dibenzyl-2,4,5-triphenyl-*trans*-imidazolinium bromide (14). Compound **7** (1 g, 2.2 mmol) was dissolved in dry acetonitrile (10 mL). 2 equiv. freshly distilled benzyl bromide (0.53 mL, 4.4 mmol) were added and the mixture was refluxed for 22 h. The colour was changing from colourless to yellow. After evaporation of the solvent the residue was dried at 60 °C under high vacuum to remove traces of benzyl bromide. Crystallization in ethyl acetate yielded the title compound **14** as a white solid (920 mg, 1.6 mmol, 74%). $[\alpha]_D^{24}$ = 132 (c = 0.50 in $CHCl_3$), mp 217 °C; ESI, m/e 479 (M^+, 100%); IR (KBr) 3030m, 3003m, 1560s, 1454s, 1286s, 751s, 736m, 698s cm^{-1}; ^{1}H NMR (200 MHz) δ 8.31–8.26 (m, 2 H, Ar–H), 7.70 (dd, J = 1.1 Hz, J = 2.4 Hz, 3 H, Ar–H), 7.45–7.34 (m, 10 H, Ar–H), 7.22 (dd, J = 1.0 Hz, J = 2.4 Hz, 6 H, Ar–H), 6.82 (dd, J = 2.2 Hz, J = 3.5 Hz, 4 H, Ar–H), 5.26 (s, 2 H, C–H), 4.69 (d, J = 15.3 Hz, 2 H, Bn–H), 4.42 (d, J = 15.3 Hz, 2 H, Bn–H); ^{13}C NMR (50 MHz) δ 167.8 (q, NCN), 133.7 (q, Ar), 133.3 (+, Ar), 132.6 (q, Ar), 130.3 (+, Ar), 130.2 (+, Ar), 129.8 (+, Ar), 129.1 (+, Ar), 129.0 (+, Ar), 128.8 (+, Ar), 128.6 (+, Ar), 122.3 (q, Ar), 73.0 (+, C(4,5)–H), 51.1 (−, CH_2). Anal. calcd for $C_{35}H_{31}N_2Br_1$: C, 75.13; H, 5.58; N, 5.01. Found: C, 74.86; H, 5.63; N, 4.74%.

(+)-(4*R*,5*R*)-1,3-Dibenzyl-2,4,5-triphenyl-*trans*-imidazolinium trifluoromethanesulfonimide (14c). Salt **14** (1 g, 1.8 mmol) was dissolved in dry dichloromethane (8 mL). 2 equiv. *N*-lithiotrifluoromethanesulfonimide (1.22 g, 3.6 mmol) were added and the mixture was stirred for 3.5 h at r.t. After adding water (8 mL) stirring was continuing for another hour, the phases were separated by using a pipette and the organic layer was washed with water (3 x 2 mL), dried (Na_2SO_4) and evaporated in vacuum. Drying under high vacuum yielded the title compound **14c** as a white solid (1.18 g, 1.6 mmol, 83%). $[\alpha]_D^{24}$ = 7 (c = 0.98 in CH_2Cl_2), mp 217 °C; ESI, m/e 479 (M^+, 100%); IR (KBr) 1591m, 1557s, 1458s, 1348s, 1323s, 1193s, 1142s, 1059s, 699s cm^{-1}; ^{1}H NMR (200 MHz) δ 8.01 (dd, J = 1.3 Hz, J = 1.6 Hz, 2 H, Ar–H), 7.90–7.78 (m, 3 H, Ar–H), 7.44 (dd, J = 0.9 Hz, J = 2.4 Hz, 6 H, Ar–H), 7.31 (dd, J = 1.1 Hz, J = 2.3 Hz, 6 H, Ar–H), 7.14 (dd, J = 2.3 Hz, J = 3.5 Hz, 4 H, Ar–H), 6.90 (dd, J = 2.2 Hz, J = 3.4 Hz, 4 H, Ar–H), 4.82 (s, 2 H, C–H), 4.73 (d, J = 15.0 Hz, 2 H, Bn–H), 4.15 (d, J = 15.0 Hz, 2 H, Bn–H); ^{13}C NMR (50 MHz) δ 166.8 (q, NCN), 134.3 (q, Ar), 134.1 (+, Ar), 131.5 (+, Ar), 131.0 (q, Ar), 130.5 (+, Ar), 130.2 (+, Ar), 129.5 (+, Ar), 129.4 (+, Ar), 129.1 (+, Ar), 128.4 (+, Ar), 127.5 (+, Ar), 121.5 (q, Ar), 71.5 (+, C(4,5)–H), 50.3 (−, CH_2). Anal. calcd for $C_{37}H_{31}N_3O_4S_2F_6$: C, 58.49; H, 4.11; N, 5.53. Found: C, 58.16; H, 4.07; N, 5.39%.

(4*R*,5*R*)-1-Benzyl-4,5-dihydro-2,4,5-triphenyl-1*H*-imidazole (16). Compound **7** (0.158 g, 0.35 mmol) was dissolved in dry acetonitrile (5 ml). Benzyl bromide (0.9 equiv.) was added, and the mixture was refluxed for 6 h. After evaporation of the solvent under reduced pressure, the residue was columned with ethyl acetate to give the title compound **16** as a colourless oil (7 mg, 0.018 mmol, 5%). ESI m/e 389.2 (M^+ + H, 100%); MS (EI), m/e 388 (M, 11%), 297 (M^+ − Bn, 20), 193 (100), 91 (Bn, 93); IR ($CHCl_3$) 3091m, 3036m, 1478s, 1036s, 637s cm^{-1}; ^{1}H NMR (200 MHz) δ 7.86–7.81 (m, 2 H, Ar–H), 7.52–7.48 (m, 3 H, Ar–H), 7.40–7.20 (m, 10 H, Ar–H), 7.14–7.09 (m, 2 H, Ar–H), 6.98–6.93 (m, 2H, Ar–H), 5.01 (d, J = 8.4 Hz, 1 H, C–H), 4.73 (d, J = 15.6 Hz, 1 H, Bn–H), 4.35 (d, J = 8.5 Hz, 1 H, C–H), 3.94 (d, J = 15.6 Hz, 1 H, Bn–H); ^{13}C NMR (50 MHz) δ 166.0 (N*C*N), 143.8 (Ar), 141.8 (Ar), 136.4 (Ar), 130.2 (Ar), 128.9 (Ar), 128.74 (Ar), 128.69 (Ar), 128.5 (Ar), 128.4 (Ar), 128.0 (Ar), 127.8 (Ar), 127.5 (Ar), 127.2 (Ar), 127.2 (Ar), 127.0 (Ar), 126.8 (Ar), 72.6 (CH), 49.6 (Bn).

(1*S*)-(−)-Camphorsulfonyl-(2-phenyl-4,5-dihydro)-imidazole (20). 2-Phenyl-4,5-dihydroimidazole (**18**) (0.8 g, 5.5 mmol) was dissolved in dry toluene (3 mL) and 1.5 equiv. triethylamine (8.25 mmol, 0.034 mL) were added. After addition of 1.2 equiv. (1*S*)-(+)-camphorsulfonic acid chloride (**19**) (6.6 mmol, 1.65 g) the solution turned into a yellowish cloudy mixture, which was stirred at r.t. for 18 h. The reaction mixture was washed with 5% aqueous HCl (3 × 2 mL) and 10% aqueous $NaHCO_3$ solution (2 × 2 mL), dried (Na_2SO_4) and evaporated under vacuum. The mixture was purified by column chromatography on SiO_2 using petroleum ether–ethyl acetate (1 : 2) as the eluent to give the crude product as a colourless oil. Recrystallisation in petroleum ether–dichloromethane gave the white pure product **20** (200 mg, 0.6 mmol, 10%). $[\alpha]_D^{24}$ = −22 (c = 1.0 in CH_2Cl_2), mp 91–95 °C; MS (EI), m/e 379 (M + H_2O, 100%); IR (KBr) 3285s, 2955s, 1742s, 1726m, 1632s, 1544s, 1328s, 1144s, 697m cm^{-1}; ^{1}H NMR (200 MHz, DMSO–D_2O) δ 8.54 (t, J = 5.4 Hz, 1 H), 7.81–7.76 (m, 2 H, Ar–H), 7.56–7.39 (m, 3 H, Ar–H), 3.38 (m, 2 H), 3.19–3.13 (m, 2 H), 2.87 (d, J = 14.9 Hz, 1 H), 2.32–2.20 (m, 2 H), 2.01 (t, J = 4.3 Hz, 1 H), 1.89–1.80 (m, 2 H), 1.56–1.27 (m, 2 H), 0.93 (s, 3 H, Me), 0.70 (s, 3 H, Me); ^{13}C NMR (50 MHz) δ 168.1 (q, C=O), 134.2 (q, Ar), 131.7 (+, Ar), 128.6 (+, Ar), 127.2 (+, Ar), 59.2 (q, C(1)), 49.6 (−, CH_2), 49.0 (q, C(7)), 43.4 (−, CH_2), 43.0 (−, CH_2), 42.8 (+, C(4)), 40.5 (−, CH_2), 27.1 (−, C(6)), 26.3 (−, C(5)), 19.9 (+, Me), 19.5 (+, Me). HRMS(ESI) found: M + H_2O + Na 401.1524. $C_{19}H_{26}N_2O_4SNa$ requires: 401.1511.

(1*S*)-(+)-Camphorsulfonyl-(2-phenyl-3-methyl)-imidazolinium iodide (21). (1*S*)-(−)-Camphorsulfonyl-(2-phenyl)-imidazole (**20**) (1.15 g, 3.2 mmol) was dissolved in dry dichloromethane (15 mL). Methyl iodide (51.2 mmol, 16 equiv., 3.2 mL) was added and the mixture was refluxed overnight. The solvent and the excess of methyl iodide were removed on the vacuum line to yield

a yellowish foam (1.3 g, 2.6 mmol, 88%). **21** was used without further purification in the anion exchange, since it was highly hygroscopic.

(1*S*)-(+)-Camphorsulfonyl-(2-phenyl-3-methyl)-imidazolinium hexafluorophosphate (21b). (1*S*)-(+)-Camphorsulfonyl-(2-phenyl-3-methyl)-imidazolinium iodide (**21**) (0.4 g, 0.78 mmol) was dissolved in dry dichloromethane (6 mL) and 1.5 equiv. potassium hexafluorophosphate (0.22 g, 1.17 mmol) was added. The mixture was stirred at r.t. overnight, quenched with water (6 mL) and stirred for an additional hour. The organic phase was washed with water (3 x 4 mL), dried (Na_2SO_4) and evaporated. Recrystallisation in ethyl acetate gave **21b** as a white solid (0.230 g, 0.4 mmol, 56%). $[a]_D^{24} = 6$ ($c = 1.05$ in CH_3CN), mp 166 °C; MS (EI), *m/e* 375 (M^+, 10%); IR (KBr) 2969m, 2929m, 1738s, 1639s, 1504m, 1445m, 1374s, 1176s, 1035m, 840s cm^{-1}; ^1H NMR (200 MHz, DMSO) δ 7.69–7.66 (m, 5 H, Ar–H), 4.52–4.16 (m, 4 H), 3.79 (d, $J = 3.8$ Hz, 1 H), 3.40 (d, $J = 2.0$ Hz, 1 H), 3.00 (s, 3 H, N–Me), 2.44–2.32 (m, 1 H), 2.05–1.89 (m, 4 H), 1.37 (d, $J = 2.0$ Hz, 2 H), 0.83 (s, 3 H, Me), 0.75 (s, 3 H, Me); ^{13}C NMR (50 MHz) δ 213.9 (q, C=O), 164.9 (q, NCN), 133.0 (+, Ar), 128.9 (+, Ar), 121.5 (q, Ar), 58.2 (q, C(1)), 51.9 (−), 48.2 (q, C(7)), 47.9 (−), 42.0 (−, C(4)), 41.9 (+, C(3)), 35.5 (+, NMe), 26.2 (−, C(6)), 24.9 (−, C(5)), 19.2 (+, Me), 19.1 (+, Me). HRMS (ESI) found: *M* 375.1756. $C_{20}H_{27}N_2O_5S$ requires: 375.1742.

Investigation of the rearrangement

Conversion of the NTf_2 salt 12c with TFA. (+)-(4*R*,5*R*)-1-Acetyl-2,4,5-triphenyl-3-methyl-*trans*-imidazolinium trifluoromethanesulfonimide (**12c**) (46 mg, 0.07 mmol) was dissolved in dry dichloromethane (1.2 mL). 20% trifluoroacetic acid in dichloromethane (0.05 mL) was added and the mixture was stirred for 24 h at r.t. After adding water (1 mL), the mixture was shaken strongly, the phases were separated and the organic layer was washed with water (2 × 1 mL), dried (Na_2SO_4) and evaporated under vacuum. Drying under high vacuum yielded a mixture consisting of the starting material **12c** and the rearrangement product **17b** as a yellowish oil (40 mg, 0.06 mmol, 87%). The rearrangement product was obtained in 78% yield according to the ^1H NMR spectra, where a ratio **12c** : **17c** = 4 : 1 was determined.

Manipulation of the PF_6 salt mixture 12b : 17b with aqueous HCl. The mixture of (+)-(4*R*,5*R*)-1-acetyl-2,4,5-triphenyl-3-methyl-*trans*-imidazolinium hexafluorophosphate (**12b**) and (+)-(4*R*,5*R*)-1-benzoyl-2,3-methyl-4,5-diphenyl-*trans*-imidazolinium hexafluorophosphate (**17b**) (20 mg, 0.04 mmol) in a ratio 1 : 2 was dissolved in dry dichloromethane (0.6 mL). 1 N aqueous hydrochloric acid (0.02 mL) was added and the mixture was stirred for 24 h at room temperature. After adding water (1 mL) the mixture was strongly shaken, the phases were separated and the organic layer was washed with water (2 × 0.5 mL), dried (Na_2SO_4) and evaporated under vacuum. Evaporation of the remaining solvent under high vacuum yielded a colourless oil (20 mg, 0.04 mmol, 100%). The ratio of the rearrangement products increased from 1 : 2 up to a ratio of 1 : 3 according to the ^1H NMR spectra.

Manipulation of the PF_6 salt mixture 12b : 17b with TFA. The mixture of (+)-(4*R*,5*R*)-1-acetyl-2,4,5-triphenyl-3-methyl-*trans*-imidazolinium hexafluorophosphate (**12b**) and (+)-(4*R*,5*R*)-1-benzoyl-2,3-methyl-4,5-diphenyl-*trans*-imidazolinium hexafluorophosphate (**17b**) (12 mg, 0.02 mmol) with a ratio of 1 : 2 was dissolved in dry dichloromethane (0.3 mL). 20% trifluoroacetic acid in dichloromethane (0.01 mL) was added and the mixture was stirred for 24 h at r.t. After adding water (1 mL) the mixture was shaken strongly, the phases were separated and the organic layer was washed with water (2 × 0.5 mL), dried (Na_2SO_4) and evaporated under vacuum. Evaporation of the remaining solvent under high vacuum yielded a colourless oil (12 mg, 0.02 mmol, 100%). The ratio of the rearrangement products increased from 1 : 2 up to 1 : 6 according to the ^1H NMR spectra.

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Imidazolinium-Carbodithioate Zwitterions as Organocatalysts for the Cyanosilylation of Aldehydes

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Abstract: Imidazolinium-carbodithioates as new organocatalysts have been found to catalyze the cyanosilylation of aldehydes in 100% conversion and good yields. The catalysts could be easily recovered during flash column chromatography.

Key words: cyanosilylation, addition, aldehydes, organocatalysis, zwitterions

The field of homogeneous catalysis is mainly dominated by metal-ligand systems,[1] but recently small simple organic molecules have attracted much interest as organocatalysts.[2] Next to the use of amino acids[3] and secondary amines[4] as covalent organocatalysts, catalysts that activate carbonyl compounds via hydrogen bondings have been found.[5] In addition, metal-free Lewis bases[6] and Lewis acids[7] have been used as catalysts. Moreover, the benzoin[8] and Stetter[9] reaction are catalyzed by organocatalysts. However, the examples so far present in the literature for organocatalysts remain small compared to metal based systems,[2] which encouraged us to present here our investigation of so far achiral imidazolinium-carbodithioate zwitterions as new organocatalysts for the addition of trimethylsilylcyanide to aldehydes.

Imidazolinium-carbodithioate zwitterions possess a Lewis acid center in the imidazolinium ring. The CS_2 group is tilted almost perpendicularly relative to the ring[10] and may be regarded as a Lewis base or Brønsted base center, although the pK_a of the corresponding acid of **3**, for example, is approximately –2.[11] These zwitterions have been used so far only rarely as ligands for metal complexes[12] and as substrates in [3+2] cycloadditions with electron deficient alkynes;[13] they have hitherto not been used as catalysts in synthesis.

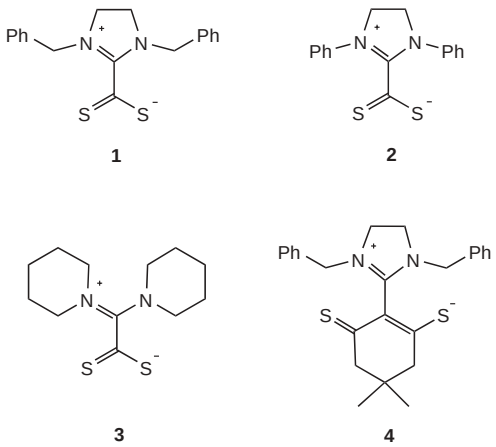
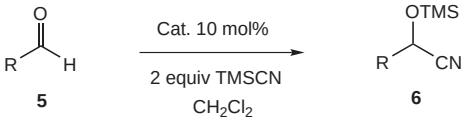


Figure 1 Catalysts for the cyanosilylation

Cyanohydrins are important intermediates in synthesis and have been mainly prepared via catalysis with metal-ligand catalysts.[14] Nevertheless, a few organocatalysts have been used like small peptides.[15] In addition, an oxazaborolidinium ion[16] and methyltriphenylphosphonium iodide[17] are known to catalyze the TMSCN addition to aldehydes. Very recently ammonium cations in combination with *N*-oxides have been applied in the silylcyanation of ketones.[18]



Scheme 1

The three zwitterions **1**,[13] **2**,[13] and **3**[11] were prepared according to literature procedures. In addition, the zwitterion **4**[19] was prepared, since it has some similarities to the other zwitterions, with the cyclohexene ring being perpendicular to the imidazolinium ring. The capability of the four zwitterions (Figure 1) for catalysis was tested in the addition of trimethylsilylcyanide to benzaldehyde (Scheme 1, Table 1).

The reactions were carried out in CH_2Cl_2 stirring benzaldehyde (1 mol/L), 2 equivalents TMSCN and 10 mol% catalyst at room temperature for 16 hours. In case of the

Table 1 Cyanosilylation of Benzaldehyde at Room Temperature in CH_2Cl_2 for 16 Hours with Different Catalysts (10 Mol%)

Entry	Catalyst	Yield (%)[a]
1	**1**	99
2	**2**	11
3	**3**	53
4	**4**	0
5	–	0

[a] Yields of isolated **6a**.

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Table 2 Cyanosilylation of Aldehydes in CH_2Cl_2 at Room Temperature with Catalyst **1** (10 Mol%) after 100% Conversion

Entry	Aldehyde		Product	Time (h)	Yield (%)[a]
1	**5a**	Benzaldehyde	**6a**	16	99
2	**5b**	3-Nitrobenzaldehyde	**6b**	16	82
3	**5c**	2-Chlorobenzaldehyde	**6c**	16	81
4	**5d**	2,4-Dichlorobenzaldehyde	**6d**	16	89
5	**5e**	2,6-Dichlorobenzaldehyde	**6e**	16	83
6	**5f**	2-Naphthaldehyde	**6f**	15	99
7	**5g**	1-Naphthaldehyde	**6g**	39	99
8	**5h**	4-Methylbenzaldehyde	**6h**	39	65
9	**5i**	2-Methylbenzaldehyde	**6i**	16	80
10	**5j**	4-Methoxybenzaldehyde	**6j**	55	82
11	**5k**	2-Methoxybenzaldehyde	**6k**	23	96
12	**5l**	Hexanal	**6l**	40	45
13	**5m**	Cyclohexanecarbaldehyde	**6m**	40	62

[a] Isolated yields after silica gel chromatography.

zwitterion **1** the starting material was all consumed and the expected product was isolated in 99% yield (entry 1, Table 1).

The catalyst **2** gave after 16 hours a yield of 11% and **3** a yield of 53%, yet not all of the aldehyde was consumed (entries 2 and 3, Table 1). Compound **4** showed no catalytic activity at all (entry 4, Table 1). A blind reaction was also carried out and as expected no conversion was detected (entry 5, Table 1). The catalysts were recovered during flash column chromatography.

With the found conditions various aldehydes were tested using catalyst **1**. The results are shown in Table 2. Next to benzaldehyde (**5a**) the electron deficient benzylic aldehydes **5b**–**f** were used and gave after 16 hours the desired products in good yields between 81% and 99% (entries 2–6). Even the more sterical hindered 2,6-dichlorobenzaldehyde (**5e**) gave the product **6e** in a good yield of 83% (entry 5, Table 2). When 1-naphthaldehyde (**5g**) was applied, the reaction time increased to 39 hours in order to observe 100% conversion. The product **6g** was obtained in an excellent yield of 99% (entry 7, Table 2). With the electron-rich benzaldehydes **5i**–**k** good yields between 80% and 96% were also obtained (entries 9–11, Table 2), but the reaction times needed for total conversion were longer in the case of 4-methoxybenzaldehyde (**5j**) with 55 hours and 2-methoxybenzaldehyde (**5k**) with 23 hours. 4-Methylbenzaldehyde (**5h**) was an exception and gave after a reaction time of 39 hours only a yield of 65% (entry 8, Table 2). A repeat of this reaction gave the same result. 2-Methylbenzaldehyde (**5i**) yielded **6i** in 80% after 16 hours (entry 9, Table 2). Finally, the reactivities of two aliphatic aldehydes were tested with the new catalytic system. Hexanal (**5l**) gave the product **6l** in 45% yield after 40 hours (entry 12, Table 2) and with cyclohexanecarbaldehyde (**5m**) the desired product **6m** was furnished in 62% yield after 40 hours (entry 13, Table 2).

In conclusion we have shown that imidazolinium-carbodithioate zwitterions are good organocatalysts in the silylcyanation of aldehydes giving the product in very good yields. The catalysts can be easily recovered. Present work within the group is investigating the behavior of asymmetric analogues of the zwitterions as organocatalysts.

General Experimental Procedure

A mixture of 1 mmol of aldehyde, 2 equiv of trimethylsilylcyanide (0.27 mL) and 10 mol% catalyst in 1 mL CH_2Cl_2 was stirred under nitrogen. The reaction was monitored by TLC until all aldehyde was consumed. After 16–55 h the solvent was evaporated and the crude product was purified by column chromatography (petrol ether–EtOAc 9:1) to give the desired compounds as slightly yellow liquids (yields: 45–99%). As a second fraction the catalyst was isolated as a deep red crystalline solid (92% yield) after changing the mobile phase to CH_2Cl_2.

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Enantiopure imidazolinium-dithiocarboxylates as highly selective novel organocatalysts†

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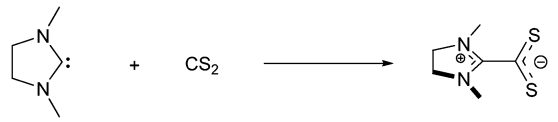
Asymmetric imidazolinium-dithiocarboxylates have been found for the first time to be highly selective catalysts; in the present case, the novel organocatalysts were able to catalyze the Staudinger reaction in up to 96% ee and 99% yield.

Imidazolinium-dithiocarboxylate[1,2] inner salts belong to the extraordinary class of carbene complexes of nonmetals.[1a] They can be formally prepared by the addition of an imidazolinium carbene to CS_2. These zwitterions are known to be stable[1,2] contrary to their CO_2 analogues.[1a,3] The CS_2 group is tilted almost perpendicularly relative to the imidazolinium ring and may be regarded as a Lewis base center (Scheme 1).

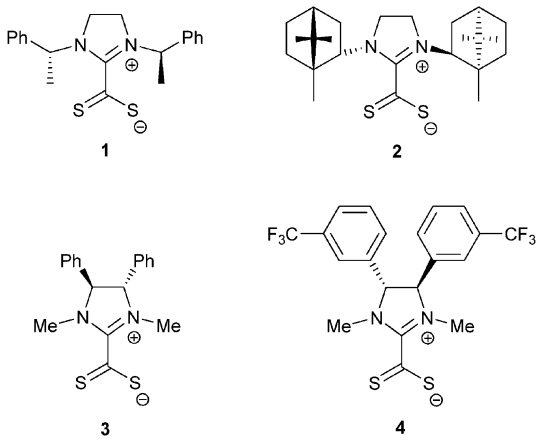
Recently, we reported the application of symmetric imidazolinium-dithiocarboxylates as catalysts for the TMSCN addition on aldehydes.[4] Due to our interest in the Staudinger reaction[5] we were wondering if the CS_2 unit of an imidazolinium-dithiocarboxylate would be a sufficient Lewis base catalyst and the positive center of the imidazolinium ring could stabilize a transition state of the intermediate. Hence, we would like to present the application of enantiopure imidazolinium-dithiocarboxylates for the first time as highly selective novel asymmetric organocatalysts[6] in the Staudinger reaction[7] for the preparation of β-lactams. Highly selective catalytic systems for the Staudinger reaction were developed by Lectka *et al.*[7a,d,f,g] using cinchona alkaloid derivatives and Fu *et al.*[7b,c] using a planar chiral ferrocene-DMAP analogue as catalyst. Recently, the groups of Ye and Smith could apply chiral carbenes in an asymmetric Staudinger reaction with either Boc protected imines with up to 99% ee and yields between 53 and 78% or tosyl protected imines in yields of up to 96% with up to 75% ee.[7g,h]

First, enantiopure imidazolinium-dithiocarboxylates depicted above were prepared. The new zwitterion **3** was prepared from its corresponding diamine[8] according to a literature procedure[2h] in 68% yield. The zwitterions **1**, **2** and **4** were synthesised from their corresponding imidazolinium salts[9] *via* two routes. Zwitterions **1** and **2** were prepared by the addition of 1 equiv. KO*t*Bu to the imidazolinium salts in order to generate the carbene in 30 min, followed by the addition of 5 equiv. of CS_2 in 43 and 74% yield, respectively. Zwitterion **4** was obtained by mixing the corresponding imidazolinium salt with 5 equiv. of CS_2 followed by the addition of 1.5 equiv. KHMDS in 54% yield after 15 min.



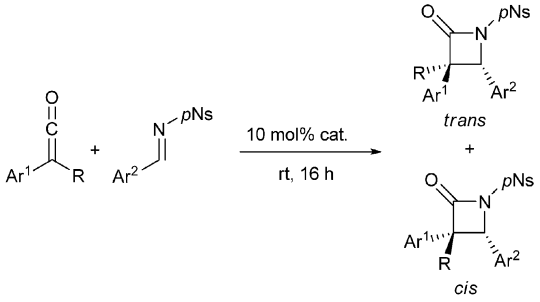
Scheme 1 Imidazolinium-dithiocarboxylates.

The [2 + 2] cycloaddition of ethylphenylketene[7c] and *N*-tosylbenzaldimine[10] was tested with zwitterion **1** in CH_2Cl_2 at rt for 16 h. However, it was not possible to isolate the desired product.



Assuming that the tosyl group is not activating the imine enough for our system, next the *para*-nosyl group[11] (4-nitrobenzenesulfonyl-), an excellent base and acid stable protecting group, which can be easily removed, was chosen. Under the given conditions with *N-para*-nosylbenzaldimine[12] the desired product was obtained in 98% yield with a *trans–cis* ratio of 62 : 38 related to the position of the two phenyl groups but with low ee (Scheme 2, Table 1, entry 1).

With the much hindered catalyst **2** no conversion was observed. Next, toluene was used as a solvent. The imine and zwitterion were not completely but sufficiently dissolved



Scheme 2 Staudinger reaction.

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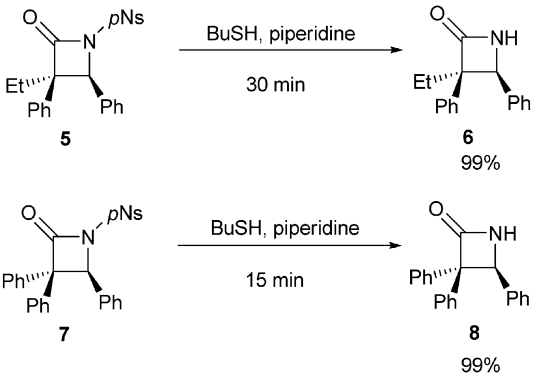
† Electronic supplementary information (ESI) available: Full experimental procedures and data. see DOI: 10.1039/b817991c

Table 1 Staudinger reaction with 1.5 equiv. ketene (Ar^1 = Ph, R = Et) and imine (Ar^2 = Ph) with 10 mol% zwitterion under various conditions in a 0.1 M solution for 16 h

Entry	Catalyst	Solvent	Yield (*trans* : *cis*)[a]	ee (*trans* : *cis*)[b]
1	**1**	CH_2Cl_2	98% (62 : 38)	6% : 4%
2	**2**	CH_2Cl_2	—	—
3	**3**	CH_2Cl_2	99% (81 : 19)	11% : 22%
4	**3**	Toluene	99% (22 : 78)	80% : 74%
5	**4**	Toluene	98% (15 : 85)	65% : 87%[c]

[a] Assignment of diastereomers *via* H-NMR CH_2 signal (*m* for *trans* and *q* for *cis*) in analogy to ref. 13. [b] Absolute configurations *trans*/*cis*: **1** (3*S*,4*S*)/(3*R*,4*S*); **3** (3*S*,4*S*)/(3*R*,4*S*); **4** (3*R*,4*R*)/(3*S*,4*R*). [c] ee could be increased to 99% through simply washing three times with 10% *i*PrOH–hexane.



Scheme 3 Deprotection of β-lactams.

to have an effective catalyst loading of 4 mol% in order to have no influence on the reaction time. However, the diastereomeric ratio shifted in favour of the *cis* diastereomer and more importantly, the obtained ee increased and gave with zwitterion **3** up to 74% ee for the major diastereomer (Table 1, entry 4). The reverse of the diastereoselectivity switching from a polar to an unpolar solvent may be explained by possible equilibriums involving ionic intermediates before the ring closing step leading in a polar solvent to the *trans* product. Zwitterion **4**, with its slightly bulkier groups in the backbone of the imidazolinium ring and its complete solubility in toluene, was prepared, which increased the ee of the *cis*-diastereomer to 87% (Table 1, entry 5). In addition, it was possible to increase the ee of this 87% ee sample to 99% ee by simply washing it three times with 10% *i*PrOH–hexane with a yield of 90%. Obviously, the racemate has a better solubility in the solvent mixture than the pure enantiomer.

With the optimized conditions, several imines and ketenes were investigated with catalyst **4** as shown in Table 2.‡ In all cases very good enantioselectivities were obtained for the *cis* isomers with up to 96%, while the *trans* isomers gave constantly lower ee with up to 83%.

Due to the difficulty of acquiring an X-ray structure in order to determine the absolute configuration of the products, the opportunity arose to show the excellent behaviour of the *p*Ns protecting group for deprotection.[11a] Therefore, samples of *cis*-**5** and **7** were prepared with *ent*-**4** and washed once with a 10% *i*PrOH–hexane mixture to give the compounds in 91 and 85% ee, respectively. However, when the standard conditions for the deprotection of a *p*Ns group were used with either $HSCH_2CO_2H$ or PhSH as nucleophiles under basic conditions, the only product obtained was due to the substitution of the nitro group with the nucleophiles. That this reaction can occur, although just as a minor side reaction, is known.[11b]

Table 2 Staudinger reaction with 1.5 equiv. ketene and imine with 10 mol% **4** in a 0.1 M solution of toluene for 16 h

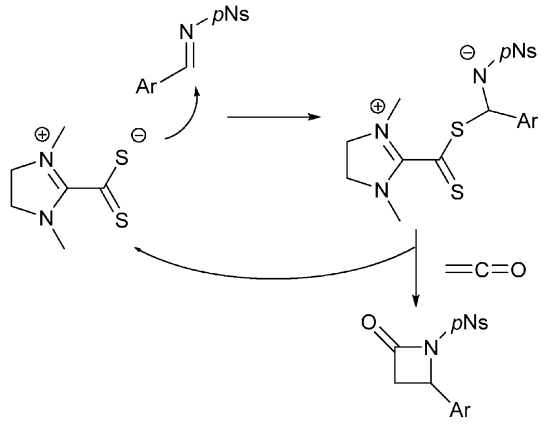
Entry	Ketene (Ar^1, R)	Imine (Ar^2)	Yield (*trans* : *cis*)	ee (*trans* : *cis*)
1	Ph, Et	2-Naphthyl	99% (14 : 86)	62% : 92%
2	Ph, Et	4-Cl-C_6H_4	98% (25 : 75)	48% : 90%
3	Ph, Et	4-CF_3-C_6H_4	96% (13 : 87)	83% : 95%
4	Ph, Et	4-NC-C_6H_4	99% (24 : 76)	74% : 93%
5	Ph, Et	4-F-C_6H_4	99% (18 : 82)	64% : 96%
6	Ph, Et	2-Thiophenyl	99% (25 : 75)	65% : 84%
7	Ph, Et	1-Naphthyl	96% (11 : 89)	70% : 83%
8	Ph, Me	4-F-C_6H_4	99% (25 : 75)	56% : 86%
9	Ph, Ph	4-F-C_6H_4	96%	76%
10[a]	Ph, Ph	Ph	96%	67%

[a] Reaction performed with *ent*-**4**.

After extensive studies it was possible to find a new procedure. As shown in Scheme 3 the protection group could be removed under mild conditions with butanethiol as solvent and piperidine to give the unprotected lactams *cis*-**6** and **8** in nearly quantitative yield. The use of butanethiol as solvent instead of DMF was essential.[11c] A possible ring opening of the lactams was not observed.[11d] The deprotected lactams were protected either with a Boc or tosyl group in order to give the literature known Boc protected lactam from *cis*-**6**[7g] and the tosyl protected lactam from **8**.[7h] By comparing the optical rotation it was possible to assign the absolute configuration. The determined ee revealed that no racemisation took place.

In order to compare the zwitterions with carbenes in the presented reaction system, a reaction was carried out with 10 mol% of the precursor salt of **3** and 9 mol% DBU in toluene with ethylphenylketene[7c] and *N*-*para*-nosylbenzaldimine.[12] After 16 h, the two diastereomers were obtained in 44% yield with a *trans*–*cis* ratio of 40 : 60. Both diastereomers were racemic. Taking into account that the base used to generate the carbene could have an influence on the outcome of the reaction, several other bases like *n*-BuLi, KO*t*Bu and KHMDS were tested. The highest ee was obtained with 10 mol% of the precursor salt of *ent*-**4** and 8 mol% KHMDS. The product was obtained in a *trans*–*cis* ratio of 40 : 60 with the *trans* product as racemate and the *cis* isomer **5** with 20% ee. These experiments should exclude the unprecedented although for many applications desirable possibility that small amounts of carbenes are generated from the zwitterions under the reaction conditions and are therefore coherent with literature.[1a]

In order to determine the possible reaction mechanism, a reaction was carried out in an NMR tube and followed over time by NMR. It was not possible to observe any shift changes of the zwitterion **3**, ketene and imine and it was only possible to observe the appearance of the product.



Scheme 4 Possible mechanism.

Therefore, the following two Lewis base catalysed sequences[7b,g,h] could be possible in the present case. Either the zwitterion is activating the ketene, which is reacting further with the imine, or it is activating the very electron deficient imine, which is reacting further with the ketene. In Scheme 4, the latter possibility is depicted.

In conclusion we have shown that the utilization of enantiopure imidazolinium-dithiocarboxylates as novel organocatalysts in the Staudinger reaction with *p*Ns protected imines can give the product in high yield and high enantiomeric excess. In addition, a procedure has been found to deprotect *p*Ns protected β-lactams in short times and high yields. Currently, the mechanism of the reaction is being further investigated.

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Notes and references

‡ *General experimental procedure for the Staudinger reaction.* An imine[12] (0.1 mmol), a ketene[7c] (0.25 mmol) and a zwitterion (10 mol%) were dissolved in dry toluene (1 ml) and left to stir for 16 h. After total conversion, the reaction mixture was applied to column chromatography on silica gel, and products were eluted with 1 : 8 diethyl ether–petrol ether mixture to give the desired compounds as white solids (yields: 96–99%). *General experimental procedure for the preparation of zwitterions.* A salt and 5 equiv. CS_2 were dissolved in THF. 1.5 equiv. KHMDS were added, and the reaction was quenched with NH_4Cl solution after 15 to 30 min. The aqueous solution was extracted with CH_2Cl_2, the solvent was removed, and the crude product was purified on silica gel.

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Hexamethyldisilazane Sodium Salt as Highly Active Lewis Base Catalyst for the Staudinger Reaction

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Abstract: Hexamethyldisilazane sodium salt (NaHMDS) has been found to be a highly active Lewis base catalyst for the Staudinger reaction with disubstituted ketenes and imines. This organocatalyst gave highly substituted β-lactams in nearly quantitative yield in a very short time of five minutes even at temperatures as low as –78 °C.

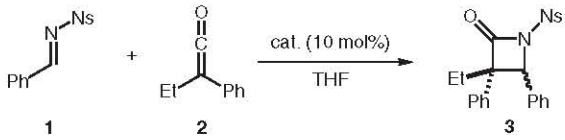
Key words: catalysis, cycloadditions, lactams, hexamethyldisilazane salts, organocatalysis, Staudinger reaction

Since its discovery, the Staudinger reaction,[1] the [2+2] cycloaddition of ketenes and imines, has proved to be an effective method to obtain racemic and enantiopure β-lactams,[2–15] which are an important class of natural compounds and antibiotics.[16–21] In addition, the obtained lactams are valuable building blocks and intermediates for synthesis toward β-amino acids.[22,23]

For the execution of the Staudinger reaction, Lewis bases are frequently applied as catalysts. The procedure may involve the interaction of N-protected imines either with freshly obtained ketenes[2,4–6] or with ketenes generated in situ from varied precursors.[2,6,7] Another approach to the synthesis of β-lactams involves utilization of a stoichiometric amount of LDA. In this case the reaction proceeds through the double deprotonation of ester enolates,[24] or by creating a lithium-centered binary or ternary complex of the lithium ester enolate, an N-protected imine and a chiral ether auxilary[25] that leads quantitatively to the cycloadduct with enantiomeric excess.

Contrary to the general usage of hexamethyldisilazane (HMDS) salts as non-nucleophilic Brønsted bases due to the sterical demanding TMS groups in the compound, utilization of these as Lewis base catalysts is barely known. In this article a synthetic pathway to β-lactams is presented that introduces hexamethyldisilazane salts as highly reactive Lewis base catalysts in the Staudinger reaction of disubstituted ketenes. To the best of our knowledge this behavior of HMDS amides as a nucleophilic catalyst in the Staudinger reaction has not been reported so far.

In the current research a set of Lewis bases was screened for the nucleophilic capacity to catalyze the Staudinger reaction (Scheme 1). Thus alkali-metal amides were tested along with strong amine bases under different reaction conditions as shown in Table 1. Due to their nucleophilic nature, best results were observed in cases, when amide catalysts were applied. Moreover, the character of the alkali metal determinated the outcome of the reaction. While NaHMDS and KHMDS resulted in total conversion at –78 °C in less than five and ten minutes, respectively (Table 1, entries 1 and 5), LiHMDS gave a moderate yield of 28% in three hours (Table 1, entry 6). Similarly, LDA catalyzed the reaction in a good yield of 77%. However, the reaction time increased to 1.5 hours, and a decrease of diastereoselectivity was observed (Table 1, entry 8). This regularity can be attributed to the lower nucleophilicity of the lithium amides, due to the stronger covalent bond character between the lithium and nitrogen.



Scheme 1 Staudinger reaction catalyzed with different catalysts

Table 1 Staudinger Reaction Catalyzed by 10 mol% of Different Catalysts at –78 °C in THF[26]

Entry	Cat.	Time	Yield (%)[a]	**3** (*trans*/*cis*)
1	KHMDS	10 min	85	1:4
2[b]		5 min	99	1:2
3[b,c]		1 h	99	1:4
4[c]		24 h	–	–
5	NaHMDS	<5 min	99	1:4
6	LiHMDS	3 h	28	1:4
7	HMDS	24 h	–	–
8	LDA	1.5 h	77	1:2.6
9	DMAP	3.5 h	92	1.2:1
10	Et_3N	24 h	17	1:1
11	DABCO	24 h	44	1:1
12[b]	DBU	24 h	traces	

[a] Yields of isolated **3**.
[b] Reaction performed at r.t.
[c] Reaction performed in toluene.

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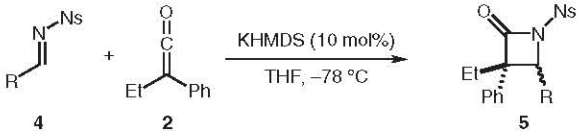
Next, reactions were carried out with commonly used tertiary amines in order to compare their reactivity to MHMDS. In all cases poor yields were obtained under the reaction conditions (Table 1, entries 9–12). The reactions of tertiary amines with such highly substituted ketenes are normally performed at room temperature or on heating and proceed over several hours.[6,27–29]

While optimizing the conditions, the reaction was performed at –78 °C in toluene, but the obtained yield of product was in range of traces. This can be mainly attributed to the poor solubility of the imines **4**.[30,31] At room temperature the reaction proceeded in toluene with quantitative yield, and the diastereomeric ratio of the product was found to be similar to that obtained at –78 °C in THF (Table 1, entry 3). The reaction performed in THF at room temperature (Table 1, entry 2) obviously resulted in a decrease of the diastereomeric ratio.



Scheme 2 Staudinger reaction with differed imines

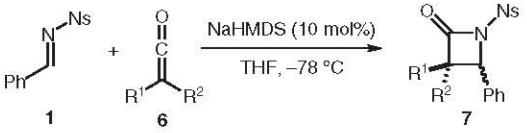
Table 2 Staudinger Reaction with Different Imines **4** and Ketene **2** Catalyzed by 10 mol% MHMDS[26]

Entry	Imine	Base	Time (min)	Yield (%)[a]	**5**[b] (*trans*/*cis*)
1	phenyl	KHMDS	10	85	**5a** (1:4)
2	phenyl	NaHMDS	<5	99	**5b** (1:4)
3	*o*-chlorophenyl	KHMDS	<3	99	**5c** (1:7)
4	*p*-tolyl	NaHMDS	<10	87	**5d** (1:2)
5	2-thiophenyl	KHMDS	15	68	**5e** (1:1.3)
6	1-naphthyl	KHMDS	90	89	**5f** (1:6.4)
7	3,4-dimethoxyphenyl	NaHMDS	120	88	**5g** (1:3.5)

[a] Isolated yields.
[b] The diastereomers were separated by column chromatography.

With these results in hand a sequence of N-protected imines was tested in the Staudinger reaction with ketene **2**[32] under the optimized conditions (Table 2, Scheme 2). The nosyl group, used for protecting the imines, was found to facilitate the formation of the β-lactams in high yield, while the tosyl-protected imine resulted in an unidentified mixture of products. Imines with electron-deficient arenes at the C2-position gave products in significant yields and diastereoselectivity with prevailing *cis*-adduct (Table 2, entries 3 and 6). Electron-rich arenes such as the 2-thiophene-derived imine formed the product **5e** with low diastereoselectivity and yield of 68% in short time. A prolong stirring after total conversion caused a decreasing of the yield (Table 2, entry 5). The electron-deficient *o*-chlorophenyl group in an imine was found to accelerate the reaction, so that the formation of the product was complete in less than three minutes (Table 2, entry 3). Due to their steric character, the *o*-chlorophenyl and naphthyl substituents enhance the diastereoselectivity for *cis*-product **5c** and **5f** (Table 2, entries 3 and 6).

Finally, some other disubstituted ketenes were applied in the reaction (Table 3, Scheme 3) in order to ascertain the influence of the size of substituents. The switch from ethyl to methyl substituent in the ketene resulted in a decrease of diastereoselectivity (Table 3, entry 1). Lower yields of **7a** and **7d** can be referred to the alternative possibility of oligomerization of the ketene. The 1,1′-diphenylketene was observed to react at room temperature in 98% yield (Table 3, entry 4).



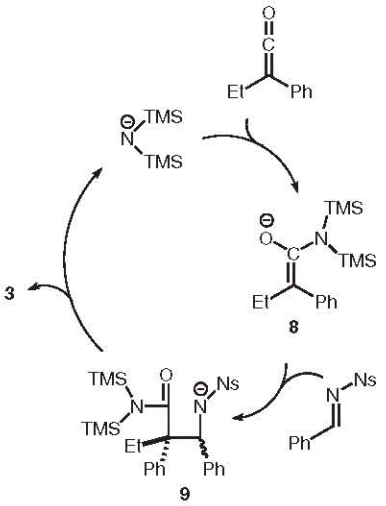
Scheme 3 Staudinger reaction with different ketenes

Table 3 Staudinger Reaction with Different Ketenes and Imine **1**[a] with 10 mol% NaHMDS[26]

Entry	Ketene	Time (min)	Yield (%)[b]	**7** (*trans*/*cis*)
1	R^1 = Ph R^2 = Me	10	72	**7a** (1:2.3)
2	R^1 = Ph R^2 = Et	5	99	**7b** (1:4)
3[c]	R^1, R^2 = Ph, Ph	180	98	**7c**
4	R^1, R^2 = cycloheptane	90	48	**7d**

[a] Reactions performed under standard conditions with NaHMDS as a catalyst.
[b] Isolated yields.
[c] Reaction performed at –78 °C to r.t.

The MHMDS-catalyzed Staudinger reaction is proposed to proceed primarily through the reaction of the Lewis base MHMDS with the ketene, leading to enolate **8** that reacts with an imine to the β-lactam (Scheme 4). In addition, another sequence could be possible. Fu recently proposed a mechanism that involves first the activation of an imine by the addition of an enantiopure DMAP–ferrocene derivative Lewis base, followed by the reaction with a ketene to the desired product.[4,5] On the base of NMR studies with NaHMDS and ketene **2** or imine **1** in deuterated THF, it was not possible to exclude either possibility, since in both cases only a large amount of decomposed material was observed. However, we can exclude a third possibility, which would start with the deprotonation of the α-proton of the imine with NaHMDS, since NMR experiments including the addition of D_2O after the addition of NaHMDS to the imine showed the α-proton of the



Scheme 4 Proposed mechanism of the Staudinger reaction catalyzed by MHMDS

imine next to the α-proton of benzaldehyde from decomposed imine.

In conclusion we have shown that the utilization of hexamethyldisilazane salts undoubtedly extended to the scope of their application as catalysts in the Staudinger reaction. The reaction was observed to be completed in a short time of 5–15 minutes at –78 °C. The procedure can be also performed at room temperature although a loss of diastereoselectivity was observed. The speed and simplicity of the reported procedure makes it a valuable tool for preparing libraries of β-lactams in parallel and combinatorial procedures for biological testing,[33] which is an important task to meet the increasing resistance of bacteria to the standard β-lactam antibiotics.[34] Current efforts within the group are directed to explore the Staudinger reaction with various enantiopure amides and other enantiopure catalysts.

Acknowledgment

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(26) **General Experimental Procedure**
An imine[30,31] (0.1 mmol) and a ketene[4,5,32] (0.25 mmol) were dissolved in dry THF (1 mL) and cooled down to –78 °C. Then, KHMDS (0.01 mmol) was added, and the reaction was monitored by TLC. After total conversion the reaction mixture was applied to column chromatography on silica gel and products were eluted with 1:8 EtOAc–PE mixture to give the desired compounds as white solids (yields: 48–99%).
Compound **5a** (*trans*-isomer): white crystals, mp 144 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.57 (t, *J* = 7.4 Hz, 3 H), 1.25–1.43 (m, 1 H), 1.64–1.89 (m, 1 H), 5.24 (s, 1 H), 7.21–7.44 (m, 10 H), 8.12 (d, *J* = 8.9 Hz, 2 H), 8.34 (d, *J* = 8.98 Hz, 2 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 8.65, 27.14, 68.07, 69.92, 124.57, 126.23, 127.21, 128.13, 128.92, 129.19, 129.26, 133.59, 137.42, 143.94, 151.03, 168.60. IR (KBr): ν = 1792 (C=O) cm^{-1}. MS (ES$^+$): *m/z* = 459.1 [M + Na]$^+$, 895.0 [2 M + Na]$^+$. Anal. Calcd (%) for $C_{23}H_{20}N_2O_5S$: C, 63.29; H, 4.62; N, 6.42. Found: C, 63.20; H, 4.67; N, 6.35.
Compound **5a** (*cis*-isomer): white crystals, mp 144–145 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.94 (t, *J* = 7.4 Hz, 3 H), 2.20 (q, *J* = 7.4 Hz, 2 H), 5.15 (s, 1 H), 6.70–6.76 (m, 2 H), 6.82–6.91 (m, 2 H), 6.94–7.16 (m, 6 H), 7.95 (d, *J* = 8.9 Hz, 2 H), 8.26 (d, *J* = 8.9 Hz, 2 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 9.31, 32.61, 69.14, 70.26, 124.40, 127.24, 127.41, 128.16, 128.19, 128.28, 128.88, 129.01, 133.66, 134.47, 144.36, 150.84, 167.80. IR (KBr): ν = 1792 (C=O) cm^{-1}. MS (ES$^+$): *m/z* = 459.1 [M + Na]$^+$, 895.0 [2 M + Na]$^+$. Anal. Calcd (%) for $C_{23}H_{20}N_2O_5S$: C, 63.29; H, 4.62; N, 6.42. Found: C, 63.38; H, 4.73; N, 6.28.

Compound **5b**: Analytical data were consistent with those for **5a**.

Compound **5c** (*trans*-isomer): white crystals, mp 107 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.83 (t, *J* = 8.0 Hz, 3 H), 2.09–2.17 (m, 1 H), 2.24–2.33 (m, 1 H), 5.64 (s, 1 H), 6.70–6.72 (m, 1 H), 6.81–6.84 (m, 1 H), 6.95–6.98 (m, 2 H), 7.03–7.07 (m, 3 H), 7.29–7.23 (m, 2 H), 8.22 (d, *J* = 8.8 Hz, 2 H), 8.43 (d, *J* = 8.8 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.31, 30.74, 64.74, 71.53, 124.78, 126.89, 128.51, 129.32, 129.41, 129.66, 132.29, 133.12, 134.10, 143.82, 151.19, 168.44. IR (KBr): ν = 1787 (C=O) cm^{-1}. MS (ES$^+$): *m/z* = 493.1 [M + Na]$^+$. Anal. Calcd (%) for $C_{23}H_{19}ClN_2O_5S$: C, 58.66; H, 4.07; N, 5.95. Found: C, 58.45; H, 4.05; N, 5.97.

Compound **5c** (*cis*-isomer): white crystals, mp 107 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.59 (t, *J* = 7.4 Hz, 3 H), 1.70 (q, *J* = 7.3 Hz, 2 H), 5.56 (s, 1 H), 7.03–7.07 (m, 5 H), 7.34–7.48 (m, 4 H), 8.15 (d, *J* = 8.8 Hz, 2 H), 8.37 (d, *J* = 8.8 Hz, 2 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 8.62, 25.4, 64.69, 69.50, 124.68, 126.65, 127.84, 128.29, 129.96, 129.22, 132.16, 133.08, 133.96, 143.60, 151.14, 168.13. IR (KBr): ν = 1793 (C=O) cm^{-1}. MS (ES$^+$): *m/z* = 493.1 [M + Na]$^+$. Anal. Calcd (%) for $C_{23}H_{19}ClN_2O_5S$: C, 58.66; H, 4.07; N, 5.95. Found: C, 58.71; H, 4.09; N, 5.81.

Compound **5d** (*trans*-isomer): white crystals, mp 142 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.57 (t, *J* = 7.4 Hz, 3 H), 1.25–1.43 (m, 1 H), 1.59–1.83 (m, 1 H), 2.39 (s, 3 H), 5.21 (s, 1 H), 7.21–7.43 (m, 9 H), 8.12 (d, *J* = 9.0 Hz, 2 H), 8.35 (d, *J* = 9.04 Hz, 2 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 8.67, 21.36, 27.17, 67.96, 69.90, 124.55, 126.24, 127.16, 128.06, 129.16, 130.50, 137.51, 139.24, 143.99, 151.06, 168.71. IR (KBr): ν = 1785 (C=O) cm^{-1}. MS (ES$^+$): *m/z* = 473 [M + Na]$^+$, 923.0 [2 M + Na]$^+$. Anal. Calcd (%) for $C_{24}H_{22}N_2O_5S$: C, 63.98; H, 4.92; N, 6.22. Found: C, 64.05; H, 5.17; N, 6.02.

Compound **5d** (*cis*-isomer): white crystals, mp 147 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.93 (t, *J* = 8.0 Hz, 3 H), 2.18 (q, *J* = 7.2 Hz, 2 H), 2.20 (s, 3 H), 5.11 (s, 1 H), 6.60 (d, *J* = 8.0 Hz, 2 H), 6.78 (d, *J* = 8.0 Hz, 2 H), 6.85–6.89 (m, 2 H), 7.02–7.09 (m, 3 H), 7.87 (d, *J* = 9.0 Hz, 2 H), 8.18 (d, *J* = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 9.31, 21.23, 32.76, 69.15, 69.98, 124.34, 127.27, 127.38, 128.17, 128.27, 128.87, 129.00, 130.54, 134.63, 138.87, 144.41, 150.76, 167.92. IR (KBr): ν = 1781 (C=O) cm^{-1}. MS (ES$^+$): *m/z* = 473 [M + Na]$^+$, 923.0 [2 M + Na]$^+$. Anal. Calcd (%) for $C_{24}H_{22}N_2O_5S$: C, 63.98; H, 4.92; N, 6.22. Found: C, 63.99; H, 5.02; N, 6.21.

Compound **5e** (*trans*-isomer): white crystals, mp 116 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.64 (t, *J* = 7.6 Hz, 3 H), 1.50–1.68 (m, 1 H), 1.85–2.03 (m, 1 H), 5.53 (s, 1 H), 7.04–7.11 (m, 2 H), 7.24–7.37 (m, 6 H), 8.10 (d, *J* = 9.0 Hz, 2 H), 8.34 (d, *J* = 9.2 Hz, 4 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 8.74, 27.65, 65.81, 68.34, 124.52, 126.24, 126.72, 127.53, 127.86, 128.24, 129.18, 129.21, 136.52, 137.08, 143.98, 168.17. IR (KBr): ν = 1782 (C=O) cm^{-1}. MS (ES$^+$): *m/z* = 465.0 [M + Na]$^+$, 907.0 [2 M + Na]$^+$, 332.1, 641.2, 774.0. Anal. Calcd (%) for $C_{21}H_{18}N_2O_5S_2$: C, 57.00; H, 4.10; N, 6.33. Found: C, 56.99; H, 4.10; N, 6.30.

Compound **5e** (*cis*-isomer): white crystals, mp 124 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.97 (t, *J* = 7.2 Hz, 3 H), 2.25 (q, *J* = 8.0 Hz, 2 H), 5.49 (s, 1 H), 6.73–6.75 (m, 2 H), 6.97–7.04 (m, 3 H), 7.11–7.18 (m, 3 H), 7.93 (d, *J* = 9.04 Hz, 2 H), 8.25 (d, *J* = 9.04 Hz, 2 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 9.33, 32.35, 64.91, 70.50, 124.35, 126.40, 127.17, 127.92, 128.54, 128.90, 129.08, 134.51, 137.21, 144.38, 150.79, 167.23. IR (KBr): ν = 1790 (C=O) cm^{-1}. MS (ES$^+$): *m/z* = 465.0 [M + Na]$^+$, 907.0 [2 M + Na]$^+$, 332.1, 641.2, 774.0. Anal. Calcd (%) for $C_{21}H_{18}N_2O_5S_2$: C, 57.00; H, 4.10; N, 6.33. Found: C, 57.13; H, 4.15; N, 6.26.

Compound **5f** (*trans*-isomer): white crystals, mp 182 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.66 (t, *J* = 7.4 Hz, 3 H), 1.26–1.43 (m, 1 H), 1.58–1.78 (m, 1 H), 5.82 (s, 1 H), 7.05–7.10 (m, 2 H), 7.34–7.38 (m, 3 H), 7.43–7.63 (m, 5 H), 7.87–7.97 (m, 2 H), 8.27 (d, *J* = 9.0 Hz, 2 H), 8.46 (d, *J* = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 8.93, 24.11, 68.46, 68.84, 122.90, 124.75, 125.08, 125.17, 126.47, 126.90, 128.55, 129.45, 129.50, 129.58, 129.67, 130.91, 133.89, 136.62, 143.99, 169.70. IR (KBr): ν = 1787 (C=O) cm^{-1}. MS (ES$^+$): *m/z* = 518.8 [(2 M + 3 Na)/2]$^+$. Anal. Calcd (%) for $C_{27}H_{22}N_2O_5S$: C, 66.65; H, 4.56; N, 5.76. Found: C, 66.77; H, 4.78; N, 5.59.

Compound **5f** (*cis*-isomer): white crystals, mp 186 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.97 (t, *J* = 7.6 Hz, 3 H), 2.26–2.47 (m, 2 H), 6.05 (s, 1 H), 6.69–6.99 (m, 6 H), 7.50–7.69 (m, 4 H), 7.83 (d, *J* = 7.8 Hz, 1 H), 8.02 (d, *J* = 8.2 Hz, 1 H), 8.15 (d, *J* = 9.0 Hz, 2 H), 8.38 (d, *J* = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 9.47, 31.21, 64.86, 71.61, 121.70, 124.65, 125.05, 126.08, 126.80, 127.17, 127.58, 128.08, 128.96, 129.34, 129.49, 129.64, 131.32, 133.45, 134.12, 138.28, 144.41, 168.62. IR (KBr): ν = 1782 (C=O) cm^{-1}. MS (ES$^+$): *m/z* = 518.8 [(2 M + 3 Na)/2]$^+$. Anal. Calcd (%) for $C_{27}H_{22}N_2O_5S$: C, 66.65; H, 4.56; N, 5.76. Found: C, 66.58; H, 4.87; N, 5.54.

Compound **5g** (*trans*-isomer): light yellow crystals, mp 143 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.59 (t, *J* = 7.4 Hz, 3 H), 1.26–1.49 (m, 1 H), 1.69–1.87 (m, 1 H), 3.86 (s, 3 H), 3.92 (s, 3 H), 5.16 (s, 1 H), 6.84 (s, 1 H), 6.88–6.89 (m, 2 H), 7.18–7.39 (m, 5 H), 8.13 (d, *J* = 9.0 Hz, 2 H), 8.35 (d, *J* = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 8.73, 27.05, 56.13, 56.19, 68.15, 69.92, 110.21, 111.25, 119.92, 124.58, 125.88, 126.18, 128.13, 129.22, 137.48, 143.91, 149.33, 149.81, 151.06, 168.80. IR (KBr): ν = 1793 (C=O) cm^{-1}. MS (ES$^+$): *m/z* = 518.8 [M + Na]$^+$, 829.0. Anal. Calcd (%) for $C_{25}H_{24}N_2O_7S$: C, 60.47; H, 4.87; N, 5.64. Found: C, 60.41; H, 4.83; N, 5.63.

Compound **5g** (*cis*-isomer): yellow crystals, mp 146 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.94 (t, *J* = 7.4 Hz, 3 H), 2.18 (q, *J* = 7.4 Hz, 2 H), 3.21 (s, 3 H), 3.79 (s, 3 H), 5.08 (s, 1 H), 5.82 (s, 1 H), 6.57–6.59 (m, 2 H), 6.84–6.92 (m, 2 H), 7.06–7.09 (m, 3 H), 7.93 (d, *J* = 9.0 Hz, 2 H), 8.26 (d, *J* = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 9.33, 32.59, 55.43, 55.93, 69.16, 69.94, 110.29, 110.62, 121.84, 124.30, 125.72, 127.24, 127.50, 128.44, 128.99, 129.18, 134.91, 144.42, 148.52, 149.53, 150.78, 167.89. IR (KBr): ν = 1787 (C=O) cm^{-1}. MS (ES$^+$): *m/z* = 518.8 [M + Na]$^+$, 829.0. Anal. Calcd (%) for $C_{25}H_{24}N_2O_7S$: C, 60.47; H, 4.87; N, 5.64. Found: C, 60.47; H, 4.90; N, 5.67.

Compound **7a** (*trans*-isomer): white crystals, mp 163 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.18 (s, 3 H), 5.28 (s, 1 H), 7.20–7.42 (m, 10 H), 8.15 (d, *J* = 9.0 Hz, 2 H), 8.37 (d, *J* = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 19.95, 64.13, 70.04, 124.61, 125.41, 126.99, 128.22, 128.98, 129.20, 129.25, 129.38, 133.58, 139.55, 143.98, 151.05, 169.08. IR (KBr): ν = 1787 (C=O) cm^{-1}. MS (ES$^+$): *m/z* = 445.1 [M + Na]$^+$, 867.0 [2 M + Na]$^+$. Anal. Calcd (%) for $C_{22}H_{18}N_2O_5S$: C, 62.55; H, 4.29; N, 6.63. Found: C, 63.19; H, 4.64; N, 6.63.

Compound **7a** (*cis*-isomer): white crystals, mp 142 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.81 (s, 3 H), 5.12 (s, 1 H), 6.71–6.77 (m, 2 H), 6.86–6.93 (m, 2 H), 6.95–7.16 (m, 6 H), 7.98 (d, *J* = 9.0 Hz, 2 H), 8.29 (d, *J* = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 25.44, 65.97, 71.10, 124.49, 126.75, 127.57, 127.91, 128.26, 128.48, 128.95, 129.08, 133.62, 135.84, 144.15, 150.94, 168.47. IR (KBr): ν = 1791 (C=O) cm^{-1}. MS (ES$^+$): *m/z* = 445.1 [M + Na]$^+$, 867.0 [2 M + Na]$^+$. Anal. Calcd (%) for $C_{22}H_{18}N_2O_5S$: C, 62.55; H, 4.29; N,

6.63. Found: C, 63.14; H, 4.60; N, 6.50.
Compound **7b**: Analytical data were consistent with those for **5a**.
Compound **7c**: white crystals, mp 156 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.86 (s, 1 H), 6.87–7.21 (m, 10 H), 7.28–7.48 (m, 5 H), 8.00 (d, *J* = 9.0 Hz, 2 H), 8.26 (d, *J* = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 69.6, 73.30, 124.44, 126.91, 127.58, 127.80, 128.03, 128.30, 128.36, 129.03, 129.07, 129.22, 133.40, 135.58, 138.72, 143.87, 150.90, 166.71. IR (KBr): ν = 1781 (C=O) cm^{-1}. MS (ES$^+$): *m/z* = 507.0 [M + Na]$^+$. Anal. Calcd (%) for $C_{27}H_{20}N_2O_5S$: C, 66.93; H, 4.16; N, 5.78. Found: C, 66.97; H, 4.31; N, 5.77.
Compound **7d**: white crystals, mp 168 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.06–1.38 (m, 4 H), 1.46–1.66 (m, 6 H), 1.72–2.02 (m, 2 H), 4.85 (s, 1 H), 7.11–7.33 (m, 5 H), 8.12 (d, *J* = 8.8 Hz, 2 H), 8.38 (d, *J* = 8.8 Hz, 2 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 22.83, 23.71, 28.98, 29.08,29.98, 35.42, 64.28, 70.50, 124.60, 127.11, 128.79, 128.98, 129.15, 134.09, 144.19, 150.99, 171.32. IR (KBr) ν = 1787 (C=O) cm^{-1}. MS (ES$^+$): *m/z* = 437.2 [M + Na]$^+$. Anal. Calcd (%) for $C_{21}H_{22}N_2O_5S$: C, 60.85; H, 5.35; N, 6.76. Found: C, 60.71; H, 5.47; N, 6.69.

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Easily Accessible Chiral Imidazolinium Salts Bearing Two Hydroxy-Containing Substituents as Shift Reagents and Carbene Precursors

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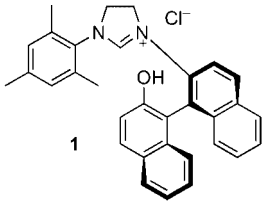
Keywords: Carbenes / Shift reagents / Ionic liquids / Imidazolinium salts

The behavior of new enantiopure imidazolinium salts bearing two hydroxy-containing substituents as chiral shift reagents and as carbene precursors for diethylzinc addition to aldehydes is presented. The new hydroxy-containing imidazolinium salts can be prepared in a few steps from amino alcohols and qualify as new tridentate ligands and ionic liquids.

Introduction

N-Heterocyclic carbenes (NHCs) have found an important role as ligands in various applications in organometallic chemistry in recent years.[1–3] In addition, various carbenes themselves can be used as organocatalysts.[4–6] The precursors of the corresponding carbenes are salts, some of which have been found to be ionic liquids, and recently a few examples of chiral ionic liquids based on chiral imidazolinium cations have been reported.[7,8] The examples of this class of chiral ionic liquids remain few in number in relation to other types of chiral ionic liquids.[9–11]

Examples of chiral imidazolinium and imidazolium salts incorporating substituents bearing hydroxy groups are rather rare. These salts act as precursors for bidentate ligands and can also be used as ionic liquids.[7] An interesting bidentate hydroxy-carbene ligand based on salt **1** was recently described by Hoveyda et al.[12] and applied with ruthenium in an asymmetric olefin metathesis, giving *ee*s of up to 96%. In addition, the carbene ligand was also investigated in a copper-catalyzed allylic alkylation, which gave the desired product in up to 98% *ee*. Furthermore, Arnold's group has synthesized salt **2**, a Cu^{I} complex with this carbene ligand having been isolated[13,14] and used as a catalyst in a diethylzinc conjugated addition to cyclohexenone, resulting in *ee*s of up to 51%. Very recently, Mauduit's group has reported the synthesis of salt **3** and has shown it to be possible to use this as a shift reagent for potassium Mosher's salt, with splittings of 60 Hz in ^{1}H NMR and 63 Hz in ^{19}F NMR spectroscopy.[7] Furthermore, the same group has also prepared salt **4** and various analogues based on different amino alcohols.[15,16] These salts were used as carbene precursors in the Cu^{II}-catalyzed addition of diethylzinc to cyclohexenone, with *ee*s of up to 93% being achieved. Moreover, the groups of Mauduit and Alexakis have used salts of type **4** together with other chiral imidazolinium salts in copper-catalyzed conjugated Grignard additions to 3-substituted cyclohexenones in order to create quaternary chiral centers, and have achieved *ee*s of up to 96%.[17]



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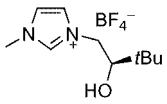

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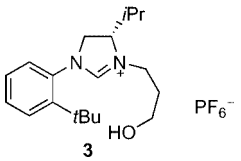

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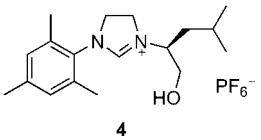

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Because of our interest in imidazolinium salts as ionic liquids[18] and catalysts[19–21] we were keen to synthesize and investigate chiral imidazolinium salts incorporating two hydroxy groups on their substituents. These salts can be prepared by the route shown in Scheme 1, and their behavior as shift reagents and carbene ligands is presented here.

Results and Discussion

The appropriate bis(amino alcohol)s were first prepared from amino alcohols and 1,2-dibromoethane by a literature procedure,[22] as shown in Scheme 1. Bis(amino alcohol) **5**, derived from (–)-norephedrine, was isolated in 79% yield, while *ent*-**5** was prepared from (+)-norephedrine in the same

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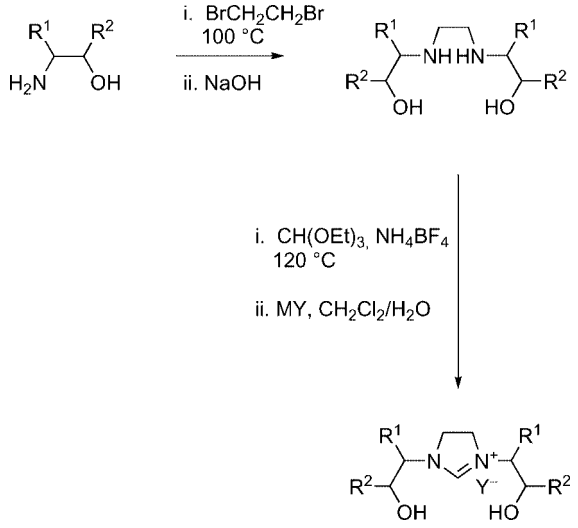


Scheme 1.

yield. The bis(amino alcohol) **6** was obtained in 77% yield from L-valinol in 77% yield, while **7** was isolated in 91% yield after treatment of L-*tert*-leucinol with dibromoethane. Finally, bis(amino alcohol) **8** was isolated in 75% yield by starting from (–)-(1*R*,2*R*)-2-amino-1-phenylpropane-1,3-diol. The bis(amino alcohol) **9** was prepared from (1*R*,2*R*)-*trans*-diaminocyclohexane and cyclohexene oxide as described in the literature.[23]

The imidazolinium salts were prepared by direct treatment of the bis(amino alcohol)s with triethyl orthoformate in the presence of NH_4BF_4 as shown in Scheme 1. Optionally, more lipophilic anions could be introduced by counteranion exchange in a mixture of chloroform and water. The reaction proceeded in high yields, as shown in Table 1. In some cases anion exchange with $LiNTf_2$ was performed, although only moderate yields were achieved here (Table 1, Entries 5 and 7). Salts **12B**, **13A**, **13C**, and **14A** could qualify as ionic liquids, since their melting points are below 100 °C,[24] while salts **10B**, **10C**, **11A**, **11B**, and **12A** could qualify as room-temperature ionic liquids.

In view of previous reports of the use of thiazolinium-,[25] imidazolinium-,[7] or ammonium-based[26] chiral ionic liquids as chiral shift reagents, and also of our investigations with chiral bis(imidazolinium)-based salts,[19] several of the prepared salts were tested for their ability to interact with Mosher's carboxylate, by examination of differences in the chemical shifts of the OMe group and the CF_3 group in the two enantiomers of Mosher's carboxylate. For these experiments, enantioenriched (12% *ee*, in order to permit the assignment of signals to the corresponding enantiomers) potassium Mosher's carboxylate **15** was mixed with the chiral imidazolinium salts in different ratios (the mixtures were dissolved in [D_6]acetone) and ^{1}H NMR and ^{19}F NMR spectra were recorded. The results are summarized in Table 2.

When enantiopure salt **10A** with a BF_4^- counteranion was used in combination with Mosher's carboxylate (Table 2, Entry 2), no signal splitting was seen either in the ^{1}H NMR or in the ^{19}F NMR spectra. On changing the counteranion to NTf_2^-, a significant increase in the splitting, to 12 Hz in the ^{1}H NMR and 118 Hz in the ^{19}F NMR, was observed (Table 2, Entry 3). A picture of these spectra is shown in Figure 1. This splitting could not be improved by use of an excess of the imidazolinium salt (Table 2, Entry 4), but the splitting was increased further, to 24 in the ^{1}H NMR and 151 Hz in the ^{19}F NMR spectra, with a change in the counteranion to $B[C_6H_3(CF_3)_2]_4^-$ (Table 2, Entry 5). To the best of our knowledge this is the largest

Table 1. Preparation of imidazolinium salts containing hydroxylated substituents.

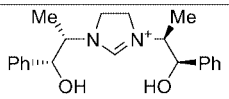
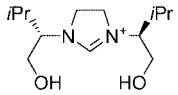
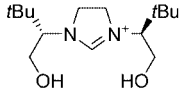
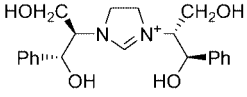
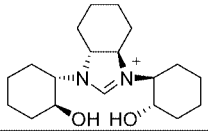
Entry	Diamine	Cation	Anion	Salt	Yield (%)
1	**5**		BF_4^-	**10A**	87
2	**5**		NTf_2^-	**10B**	93
3	**5**		$B[C_6H_3(CF_3)_2]_4^-$	**10C**	85
4	**6**		BF_4^-	**11A**	94
5	**6**		NTf_2^-	**11B**	52
6	**7**		BF_4^-	**12A**	88
7	**7**		NTf_2^-	**12B**	59
8	**8**		BF_4^-	**13A**	98
9	**8**		$B[C_6H_3(CF_3)_2]_4^-$	**13C**	80
10	**9**		BF_4^-	**14A**	93

Table 2. Chemical shifts δ of Mosher's carboxylate in ppm and $\Delta\delta$ values in Hz (400 MHz NMR spectroscopy).

Entry	Salt	Ratio	$\delta(^1H)$		$\delta(^{19}F)$		$\Delta\delta(^1H)$	$\Delta\delta(^{19}F)$
			(*S*)	(*R*)	(*S*)	(*R*)		
1	–	N/A	3.54	3.54	–71.59	–71.59	0	0
2	**10A**	1:1	3.54	3.54	–71.59	–71.59	0	0
3	**10B**	1:1	3.55	3.52	–70.90	–71.22	12	118
4	**10B**	3:1	3.55	3.52	–70.90	–71.22	12	118
5	**10C**	1:1	3.50	3.56	–71.39	–70.99	24	151
6	**11A**	1:1	3.590	3.587	–71.65	–71.70	1.2	18
7	**11B**	1:1	3.58	3.58	–71.63	–71.60	0	15
8	**13C**	1:1	3.55	3.55	–71.52	–71.50	0	7
9	**14A**	1:1	3.60	3.60	–71.32	–71.41	0	32

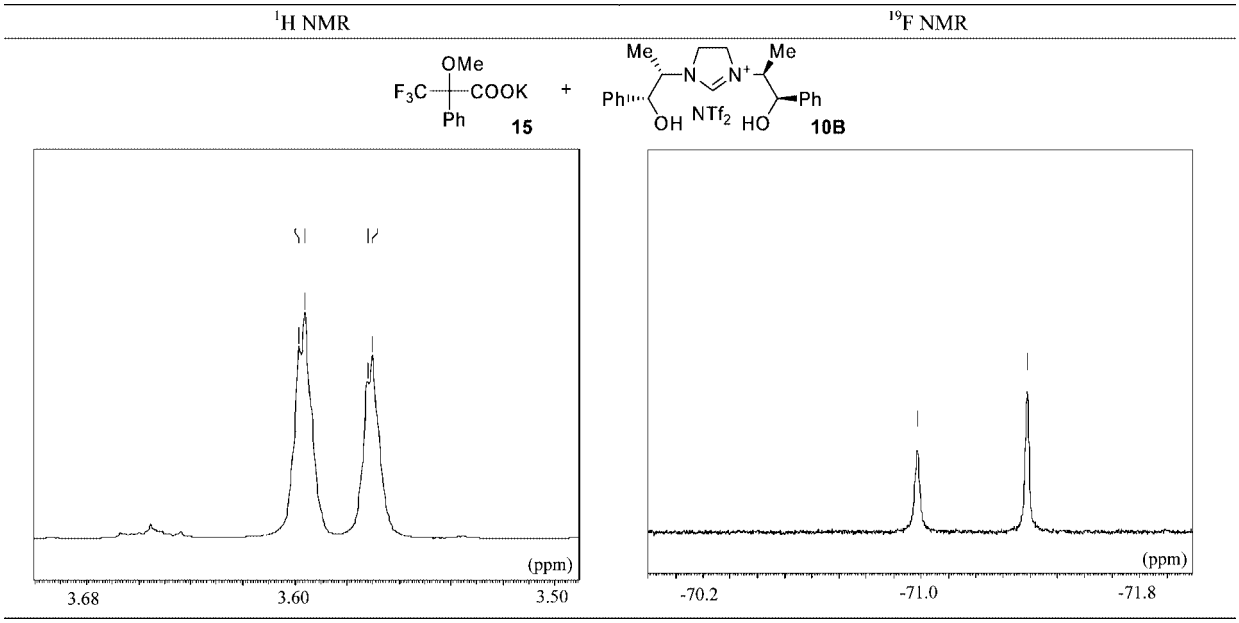
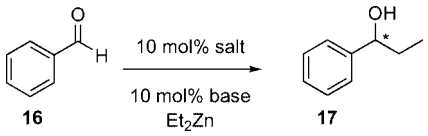


Figure 1. NMR spectra of salt **10B** with potassium Mosher's carboxylate (**15**).

reported ^{19}F NMR signal splitting obtained with an imidazolinium salt.

Salt **11A** showed a poor splitting, 1.2 Hz in the ^{1}H NMR and 18 Hz in the ^{19}F NMR (Table 2, Entry 6), while a change in the counteranion to NTf_2^- did not in this case result in any improved splitting (Table 2, Entry 7). Salt **13C**, with a $B[C_6H_3(CF_3)_2]_4^-$ moiety, showed no splitting in its ^{1}H NMR spectrum and a poor splitting of 7 Hz in its ^{19}F NMR spectrum (Table 2, Entry 9), while the BF_4^- salt **14A** displayed a splitting of 32 Hz in its ^{19}F NMR signal. An upfield shift of the signal in the ^{1}H NMR indicated interactions between the imidazolinium cation and the Mosher's salt, but no stereodiscrimination was observed (Table 2, Entry 9).

In order to demonstrate that the new imidazolinium salts bearing two hydroxy-containing substituents are potential new carbene ligands, they were tested in diethylzinc addition to aldehydes. This enantioselective C–C bond formation for the preparation of optically active secondary alcohols has been intensely studied with various catalytic systems.[27–29] The salts were first tested in the addition of diethylzinc to benzaldehyde (**16**), as shown in Scheme 2, the reactions being performed at room temperature and different solvents being tested. The results are summarized in Table 3.



Scheme 2.

In order to generate the carbene, imidazolinium salt **14A** was deprotonated with *t*BuOK in a PhMe solution. After 5 min of stirring, Et_2Zn (1.1 equiv.) was added, followed by benzaldehyde (1 equiv.). After 30 h of stirring at room temp. and quenching of the reaction mixture with HCl (1 M), the product was isolated in 67% yield and showing 66% *ee* (Table 3, Entry 2). When no base was present, no reaction occurred, indicating that the carbene generation is essential for the reaction to proceed (Table 3, Entry 1). The mechanism of the reaction has been thoroughly examined in the case of β-amino alcohol ligands.[30,31] In the present case, the carbene unit is probably taking over the role of the amine substituent of a β-amino alcohol.

Table 3. Addition of Et_2Zn to benzaldehyde (**16**).

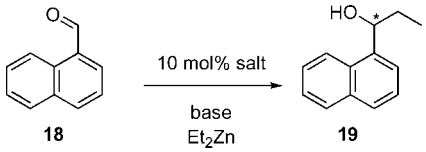
Entry	Catalyst	Solvent	Base	Yield [%]	*ee* [%]	Configuration
1	**14A**	PhMe	–	0	–	–
2	**14A**	PhMe	*t*BuOK	67	66	(*R*)
3	**10A**	THF	*t*BuOK	traces	–	–
4	**10A**	DME	*t*BuOK	0	–	–
5	**10A**	dioxane	*t*BuOK	0	–	–
6	***ent*-10A**	PhMe	*t*BuOK	57	40	(*S*)
7	**11A**	PhMe	*t*BuOK	38	35	(*R*)
8	**12A**	PhMe	*t*BuOK	70	8	(*R*)

Table 4. Addition of Et_2Zn to 1-naphthaldehyde (**18**).

Entry	Catalyst	Base	*T* [°C]	Yield [%]	*ee* [%]	Configuration
1	**10A**	*t*BuOK (0.1 equiv.)	room temp.	61	60	(*R*)
2	**10A**	KHMDS (0.1 equiv.)	room temp.	92	45	(*R*)
3	**10A**	KHMDS (0.2 equiv.)	room temp.	84	45	(*R*)
4	**10A**	KHMDS (0.3 equiv.)	room temp.	78	31	(*R*)
5	**10A**	KHMDS (0.1 equiv.)	–5	85	55	(*R*)
6	**10A**	KHMDS (0.1 equiv.)	–78	traces	–	–
7	**10A**	NaHMDS (0.1 equiv.)	room temp.	80	47	(*R*)
8	**10A**	LiHMDS (0.1 equiv.)	room temp.	76	36	(*R*)
9	**13A**	KHMDS (0.1 equiv.)	room temp.	60	33	(*R*)
10	**14A**	KHMDS (0.1 equiv.)	–25	58	25	(*R*)

Next, salt **13A** was tested in various solvents. In DME and dioxane the reaction did not give any product, while a reaction in THF gave only traces (Table 3, Entries 3–5). Finally, the reaction in PhMe gave the corresponding product in 57% yield and with 40% *ee* (Table 3, Entry 6). The L-valinol-based compound **11A** gave the alcohol **17** in 38% yield and with 35% *ee* (Table 3, Entry 7). Changing the *i*Pr groups to *t*Bu groups in catalyst **12A** resulted in an increase of the yield to 70% but an *ee* of only 8% was detected (Table 3, Entry 8).

1-Naphthaldehyde (**18**) was also used, as shown in Scheme 3, and the influence of different bases was investigated. The results are presented in Table 4.



Scheme 3.

When the reaction was conducted with catalyst **10A** in the presence of *t*BuOK as a base, the corresponding alcohol **19** was isolated in 61% yield and with 60% *ee* (Table 4, Entry 1). Changing the base to KHMDS resulted in a dramatic increase in the yield to 92%, but the *ee* decreased to 45% (Table 4, Entry 2). Use of 2 and 3 equiv. of the base resulted in decreases in the yield to 84 and 78%, respectively, while in the case of 3 equiv. the *ee* dropped to 31% (Table 4, Entries 3 and 4). If the reaction temperature was decreased to –5 °C, the yield decreased slightly to 85%, but the *ee* increased to 55% (Table 4, Entry 5). After a further reduction in temperature to –78 °C, only traces of compound **19** were isolated (Table 4, Entry 6). Performing the reaction with use of different hexamethyldisilazane salts resulted in yields of 80 and 76% and *ee*s of 47 and 33% (Table 4, Entries 7 and 8), showing that potassium is the best countercation for this type of reaction.

In order to show that the formed carbenes were stable under the optimized conditions, salt **10A** was dissolved in toluene. After the addition of *t*BuOK, diethylzinc was added and the solution was stirred overnight. After aqueous workup and extraction, salt **10A** was recovered and identified by ^1H NMR spectroscopy.

Conclusion

We have presented the preparation of a series of new, enantiopure imidazolinium salts bearing two hydroxylated substituents, which were shown to be efficient and reusable shift reagents for Mosher's carboxylate. In addition, they can be used as carbene ligands for the enantioselective addition of Et_2Zn to aldehydes and also qualify as new chiral ionic ligands. Further applications of this new class of potential tridentate ligands are currently being investigated in our group, and these will be reported soon.

Experimental Section

General Experimental: Flash column chromatography[32] was performed on Sorbisil C-60. Reactions were monitored by TLC on Merck silica gel 60 F254 plates. Elemental analysis were carried out by the Microanalytical Laboratory of the Institut für Pharmazeutische Chemie der Technische Universität Braunschweig with an Elemental Analyzer Model 1106 from Carlo Erba Instrumentazione. Infrared spectra were recorded with a Bruker Vektor 22 FTIR spectrometer, as KBr pellets in cases of solid compounds and as thin films between NaCl plates in cases of oils and liquids. ^1H NMR spectra were recorded at ambient temperature

with Bruker AMX 400 (400 MHz) and AC 200F (200 MHz) instruments with tetramethylsilane as internal standard. ^{13}C NMR spectra were recorded at ambient temperature with Bruker AMX 400 (100 MHz) and AC 200F (50 MHz) instruments and ^{19}F NMR spectra were recorded at ambient temperature with a Bruker AMX 400 (378 MHz) instrument. Mass spectra (ESI) were recorded with a Hewlett–Packard MS LC/MSD Series 1100 MSD instrument, while high-resolution mass spectra were measured with a Bruker Daltonik Tesla–Fourier Transform-Ion Cyclotron Resonance Mass Spectrometer. Melting points were taken with a Dr. Tottoli apparatus and are uncorrected. Reactions were performed under nitrogen. All solvents were dried by standard procedures before used in the reactions. L-Valinol,[33] L-*tert*-leucinol,[34] sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate,[35] (1*R*,2*S*)-2-({2-[(1*S*,2*R*)-2-hydroxy-1-methyl-2-phenylethylamino]ethyl}-amino)-1-phenylpropan-1-ol (**5**)[22] and compound **9**[23] were prepared according to literature procedures. (–)-Norephedrine, (+)-norephedrine, (–)-(1*R*,2*R*)-amino-1-phenylpropane-1,3-diol, aldehydes, potassium *tert*-butoxide, lithium bis(trifluoromethylsulfonyl)imide, and diethylzinc were purchased from Aldrich. Mosher's reagent was purchased from Lancaster.

Preparation of Diamines

General Procedure for the Preparation of Diamines by Alkylation with $BrCH_2CH_2Br$:[22] An amino alcohol (1.00 mmol) and dibromoethane (87 μL, 0.50 mmol) were placed in a pressure vessel, which was flushed with nitrogen and sealed. The reaction mixture was heated at 100 °C for 10 h, during which the reaction mixture solidified. After the system had cooled to room temp., the solid was dissolved in water (10 mL) and the aqueous phase was washed with $CHCl_3$ (3 × 3 mL). The aqueous phase was basified with NaOH (40 mg, 1 equiv.) and the precipitated free base was extracted with $CHCl_3$ (3 × 5 mL). The combined organic fractions were dried (Na_2SO_4) and the solvent was removed under reduced pressure to give the pure bis(amino alcohol).

(1*S*,2*R*)-2-[(2-{[(1*R*,2*S*)-2-Hydroxy-1-methyl-2-phenylethyl]amino}-ethyl)amino]-1-phenylpropan-1-ol (*ent*-5): This compound was prepared from (+)-norephedrine (5.01 g, 33.00 mmol) and dibromoethane (1.42 mL, 16.50 mmol), after basification with NaOH (2 M, 14.00 mL, 28.00 mmol), as a yellow oil (4.15 g, 79%). Spectral data are consistent with literature values.[36]

(*S*)-2-[(2-{[(*S*)-1-(Hydroxymethyl)-2-methylpropyl]amino}ethyl)-amino]-3-methylbutan-1-ol (6): This compound was prepared from L-valinol (1.23 g, 11.90 mmol) and dibromoethane (513 μL, 5.95 mmol), after basification with NaOH (2 M, 5.10 mL, 10.20 mmol), as a yellow oil (1.06 g, 77%). $[a]_D^{22}$ = +14.3 (*c* = 0.65, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ = 3.67–3.59 (m, 2 H), 3.42–3.33 (m, 2 H), 2.90–2.50 (m, 4 H), 2.40–2.25 (m, 2 H), 1.90–1.70 (m, 2 H), 1.01–0.85 (m, 12 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 65.2, 62.0, 47.4, 29.4, 20.1, 18.7 ppm. IR (neat): $\tilde{\nu}$ = 3314 s, 2958 s, 2873 s, 1467 s, 1052 s, 452 s cm^{-1}. MS (ESI = 0 V): *m*/*z* (%) = 233.3 (100) $[M + H]^+$. The preparation of this compound by the reduction of a bis(amide) had previously been reported,[37] but no spectroscopic data were provided.

(*S*)-2-[(2-{[(*S*)-1-(Hydroxymethyl)-2-methylpropyl]amino}ethyl)-amino]-3-methylbutan-1-ol (7): This compound was prepared from L-*tert*-leucinol (2.00 g, 17.10 mmol) and dibromoethane (740 μL, 8.55 mmol), after basification with NaOH (2 M, 8.55 mL, 17.10 mmol), as a white solid (2.01 g, 91%). For elemental analysis the diamine was crystallized from EtOH; m.p. 53 °C. $[a]_D^{22}$ = +53.8 (*c* = 0.34, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 3.71 (dd, *J* = 3.52, 10.6 Hz, 2 H), 3.55–3.42 (m, 2 H), 3.08 (d, *J* = 8.6 Hz), 2.73 (d, *J* = 8.6 Hz), 2.34 (dd, *J* = 3.52, 10.6 Hz, 2 H), 0.97 (s, 18 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 67.9, 62.9, 49.7, 34.4, 27.2 ppm. IR (KBr): $\tilde{\nu}$ = 3314 s, 2958 s, 2873 s, 1467 s, 1052 s, 452 s cm^{-1}. MS (EI): *m*/*z* (%) = 261 (10) $[M + H]^+$, 229 (15), 203 (25), 144 (25), 130 (100), 100 (50), 86 (50), 74 (40), 57 (45). HRMS (ESI): calcd. for $C_{14}H_{33}N_2O_2$ 261.2542; found 261.2546. $C_{14}H_{32}N_2O_2$ (260.4): C 64.57, H 12.39, N 10.76; found C 64.44, H 12.54, N 10.88.

(1*R*,1′*R*,2*R*,2′*R*)-2,2′-[Ethane-1,2-diylbis(azanediyl)]bis(1-phenylpropane-1,3-diol) (8): This compound was prepared from (–)-(1*R*,2*R*)-2-amino-1-phenylpropane-1,3-diol (1.15 g, 6.89 mmol) and dibromoethane (296 μL, 3.45 mmol) as a yellow oil (930 mg, 75%). $[a]_D^{22}$ = –78.2 (*c* = 0.28, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.45–7.30 (m, 10 H), 4.60 (d, *J* = 7.6 Hz, 2 H), 3.65–3.55 (m, 2 H), 3.35–3.25 (m, 2 H), 2.80–2.60 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.0, 128.5, 127.8, 126.7, 73.8, 64.8, 60.2, 46.8 ppm. IR (neat): $\tilde{\nu}$ = 3356 vs, 2882 s, 1454 s, 1027 s, 759 vs, 702 vs cm^{-1}. MS (ESI = 0 V): *m*/*z* (%) = 361.0 (70) $[M + H]^+$. HRMS (ESI): calcd. for $C_{20}H_{29}N_2O_4$ 361.2127; found 361.2122.

General Procedure for Preparation of Imidazolium Tetrafluroborate Salts: A bis(amino alcohol) (1.00 mmol) was placed in a flask, and the counteranion source (typically NH_4BF_4, 1.00 mmol) and either triethyl orthoformate (148 mg, 165 μL, 1.00 mmol) or triethyl orthoacetate (127 μL 97%, 0.66 mmol) was added. The reaction vessel was flushed with nitrogen and sealed, and the mixture was heated to 120 °C for 2 h. After cooling, the mixture was dried under vacuum, in order to remove ethanol, formed during the reaction, to give the crude salt in high purity. Optionally, the product was crystallized from absolute ethanol.

General Procedure for the Counteranion Exchange with Lithium Bis-(trifluoromethylsulfonyl)imide: An imidazolinium tetrafluoroborate salt (1.00 mmol) was dissolved in CH_2Cl_2 (3 mL) and the mixture was vigorously stirred with a solution of $LiNTf_2$ (1.00 mmol) in water (3 mL) for 3 h. The organic phase was separated, washed with water (3 × 3 mL), and dried with molecular sieves (3 Å). The solvent was evaporated and the product was further dried under vacuum to give the corresponding imidazolinium bis(trifluoromethylsulfonyl)imide salt.

General Procedure for the Counteranion Exchange with Sodium Tetrakis[3,5-bis(trifluoromethyl)phenyl]borate: An imidazolinium tetrafluroborate (1.00 mmol) was dissolved in CH_2Cl_2 (3 mL), and $NaB[C_6H_3(CF_3)_2]_4$ (1.00 mmol, 1 equiv.) and water (3 mL) were added sequentially. The reaction mixture was then vigorously stirred for 3 h. The organic phase was separated (centrifugation was used to improve separation if separation did not occur), washed with water (3 × 3 mL), and dried with molecular sieves (3 Å). The solvent was evaporated and the product was further dried in vacuo to give the corresponding imidazolinium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate salt.

1,3-Bis[(1*R*,2*S*)-2-hydroxy-1-methyl-2-phenylethyl]imidazolinium Tetrafluoroborate (10A): This compound was prepared from **5** (657 mg, 2.00 mmol), NH_4BF_4 (216 mg, 2.00 mmol), and $CH(OEt)_3$ (326 μL, 2.00 mmol) as described in the General Procedure. The reaction mixture was heated to 120 °C in a sealed vessel for 8 h, giving the title compound as a yellow solid (743 mg, 87%); m.p. 162 °C. $[a]_D^{22}$ = +17.9 (*c* = 1.2, MeOH). ^1H NMR (200 MHz, [D$_6$]DMSO): δ = 8.32 (s, 1 H), 7.50–7.20 (m, 10 H), 5.95 (br. s, 2 H), 4.81 (d, *J* = 4.0 Hz, 2 H), 4.00–3.70 (m, 6 H), 1.08 (d, *J* = 6.9 Hz) ppm. ^{13}C NMR (50 MHz, [D$_6$]DMSO): δ = 156.2, 141.4, 128.1, 127.4, 126.1, 72.7, 58.6, 47.0, 12.1 ppm. IR (KBr): $\tilde{\nu}$ = 3273 s, 1652 vs, 1265 s, 1139 s, 1070 vs, 1015 s, 988 s, 704 s cm^{-1}. MS (ESI = 0 V): *m*/*z* (%) = 339 (100) $[M]^+$. HRMS (ESI): calcd for $C_{21}H_{27}N_2O_2^+$ 339.2073; found 339.2074.

1,3-Bis[(1*S*,2*R*)-2-hydroxy-1-methyl-2-phenylethyl]imidazolinium Tetrafluoroborate (*ent*-10A): This compound was prepared in the same manner, from ***ent*-5**.

1,3-Bis[(1*R*,2S)-2-hydroxy-1-methyl-2-phenylethyl]imidazolinium Bis(trifluoro-methylsulfonyl)imide (10B): This compound was prepared from **10A** (300 mg, 0.70 mmol) and $LiNTf_2$ (208 mg, 97%, 0.70 mmol) in a mixture of dichloromethane (DCM) (5 mL) and water (5 mL), as a yellow oil (404 mg, 93%). $[a]_D^{22}$ = +20.8 (*c* = 0.9, MeOH). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.78 (s, 1 H), 7.37–7.20 (m, 10 H), 4.96 (d, *J* = 3.2 Hz, 2 H), 4.00–3.70 (m, 4 H), 3.16 (br. s, 2 H), 1.17 (d, *J* = 7.0 Hz, 6 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 155.6, 139.2, 128.7, 128.3, 125.9, 73.6, 59.5, 47.6, 12.2 ppm. IR (neat): $\tilde{\nu}$ = 3523 s, 1642 vs, 1352 vs, 1197 vs, 1137 vs, 1057 vs, 706 s, 617 s, 442 vs cm^{-1}. MS (ESI = 0 V): *m*/*z* (%) = 339.2 (100) $[M]^+$. HRMS (ESI): calcd. for $C_{21}H_{27}N_2O_2^+$ 339.2073; found 339.2073.

1,3-Bis[(1*S*,2*R*)-2-hydroxy-1-methyl-2-phenylethyl]imidazolinium Bis(trifluoro-methylsulfonyl)imide (*ent*-10B): This compound was prepared in the same manner, from ***ent*-10A**.

1,3-Bis[(1*R*,2*S*)-1-hydroxy-1-phenylpropan-2-yl]imidazolinium Tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (10C): This compound was prepared from **10A** (200 mg, 0.47 mmol) and $NaB[C_6H_3(CF_3)_2]_4$ (416 mg, 0.47 mmol) in a mixture of DCM (5 mL) and water (5 mL), as a brown oil (477 mg, 84%). $[a]_D^{22}$ = –53.2 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $[D_6]$acetone): δ = 8.33 (s, 1 H), 7.08 (br. s, 8 H), 7.69 (br. s, 4 H), 7.50–7.30 (m, 10 H), 5.20–5.05 (m, 2 H), 4.25–4.05 (m, 6 H), 2.88 (br. s, 2 H), 1.29 (d, *J* = 8.1 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $[D_6]$acetone): δ = 161.7 (q, *J* = 49.5 Hz), 156.4, 140.9, 134.6, 129.3 (q, *J* = 28.4 Hz), 128.4, 127.9, 126.2 124.5 (q, *J* = 269.8 Hz), 117.6, 73.8, 59.6, 52.5, 47.8, 47.6, 12.1 ppm. IR (KBr): $\tilde{\nu}$ = 1641 m, 1356 s, 1279 vs, 1124 vs, 682 m cm^{-1}. MS (ESI = 0 V): *m*/*z* (%) = 339.2 (100) $[M]^+$. HRMS (ESI): calcd. for $C_{21}H_{27}N_2O_2^+$ 339.2073; found 339.2079.

1,3-Bis[(*S*)-1-(hydroxymethyl)-2-methylpropyl]-4,5-imidazolinium Tetrafluoroborate (11A): This compound was prepared from **6** (12 mg, 1.34 mmol), NH_4BF_4 (141 mg, 1.34 mmol), and $CH(OEt)_3$ (220 μL, 1.34 mmol) as described in the General Procedure, as a yellow oil (418 mg, 94%). $[a]_D^{22}$ = –10.6 (*c* = 0.68, acetone). ^{1}H NMR (200 MHz, $[D_6]$acetone): δ = 8.20 (s, 1 H), 4.07 (br. s, 2 H), 4.00–3.85 (m, 4 H), 3.75–3.25 (m, 6 H), 2.00–1.70 (m, 2 H), 0.91 (d, *J* = 6.5 Hz, 12 H) ppm. ^{13}C NMR (50 MHz, $[D_6]$acetone): δ = 160.1, 67.5, 59.8, 46.2, 27.9, 20.1, 19.4 ppm. IR (neat): $\tilde{\nu}$ = 3548 s, 2968 s, 2881 s, 1644 vs, 1472 s, 1394 s, 1254 s, 1074 vs, 446 s cm^{-1}. MS (ESI = 0 V): *m*/*z* = 243.2 [cation]. HRMS (ESI): calcd. for $C_{13}H_{27}N_2O_2^+$ 243.2073; found 243.2073.

1,3-Bis[(*S*)-1-(hydroxymethyl)-2-methylpropyl]-4,5-imidazolinium Bis(trifluoromethylsulfonyl)imide (11B): This compound was prepared from **11A** (235 mg, 0.71 mmol) and $LiNTf_2$ (204 mg, 0.71 mmol, 1 equiv.) in a mixture of DCM (5 mL) and water (5 mL), as a yellow oil (197 mg, 52%). $[a]_D^{22}$ = –18.9 (*c* = 0.28, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.16 (s, 1 H), 4.00–3.80 (m, 4 H), 3.70–3.30 (m, 4 H), 3.09 (br. s, 2 H), 2.00–1.75 (m, 2 H), 0.99 (d, *J* = 6.7 Hz, 12 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 159.2, 66.9, 59.4, 45.3, 27.6, 19.7, 18.9 ppm. IR (neat): $\tilde{\nu}$ = 3537 m, 2971 s, 1644 vs, 1352 vs, 120 vs, 1137 vs, 1058 vs, 617 vs cm^{-1}. MS (ESI = 0 V): *m*/*z* = 243.3 $[M]^+$. HRMS (ESI): calcd. for $C_{13}H_{27}N_2O_2^+$ 243.2073; found 243.2077.

1,3-Bis[(*S*)-1-hydroxy-3,3-dimethylbut-2-yl]imidazolinium Tetrafluoroborate (12A): This compound was prepared from **7** (1.00 g, 3.85 mmol), NH_4BF_4 (615 mg, 3.85 mmol), and $CH(OEt)_3$ (633 μL, 3.85 mmol). The reaction mixture was heated at 120 °C for 8 h and standard workup gave the title compound as a colorless oil (1.30 g, 88%). $[a]_D^{22}$ = +24.4 (*c* = 0.46, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15 (s, 1 H), 4.20–4.10 (m, 2 H), 4.10–4.00 (m, 2 H), 3.95 (dd, *J* = 3.7, 12.3 Hz, 2 H), 3.82 (t, *J* = 10.8 Hz, 2 H), 3.60 (dd, *J* = 3.7, 12.3 Hz), 1.04 (s, 18 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.2, 69.9, 57.8, 49.7, 33.8, 27.3 ppm. IR (neat): $\tilde{\nu}$ = 3541 s, 2967 vs, 1699 m, 1639 vs, 1479 s, 1409 m, 1373 s, 1283 s, 1237 m, 1058 vs, 451 s, 415 m, 406 m cm^{-1}. MS (ESI = 0 V): *m*/*z* = 271.3 $[M(cation)]^+$. HRMS (ESI): calcd. for $C_{15}H_{31}N_2O_2^+$ 271.2386; found 271.2396.

1,3-Bis[(*S*)-1-hydroxy-3,3-dimethylbut-2-yl]imidazolinium Bis(trifluoromethylsulfonyl)imide (12B): This compound was prepared from **12A** (294 mg, 0.86 mmol) and $LiNTf_2$ (246 mg, 0.86 mmol, 1 equiv.) in a mixture of DCM (5 mL) and water (5 mL), as a white solid (277 mg, 59%); m.p. 98 °C. $[a]_D^{22}$ = +19.7 (*c* = 0.36, $CHCl_3$). ^{1}H NMR (200 MHz, $[D_6]$acetone): δ = 8.36 (s, 1 H), 4.25–4.05 (m, 4 H), 4.00–3.80 (m, 4 H), 3.60–3.45 (m, *J* = 10.8 Hz, 2 H), 0.93 (s, 18 H) ppm. ^{13}C NMR (50 MHz, $[D_6]$acetone): δ = 161.7, 121.0 (q, *J* = 319.5 Hz), 70.9, 57.9, 48.8, 34.4, 27.5 ppm. IR (KBr): $\tilde{\nu}$ = 3423 s, 1637 s, 1194 s, 1057 s cm^{-1}. MS (ESI = 0 V): *m*/*z* = 271.3 $[M]^+$. HRMS (ESI): calcd for $C_{15}H_{31}N_2O_2$ 271.2386; found 271.2381.

1,3-Bis[(1*R*,2*R*)-1,3-dihydroxy-1-phenylprop-2-yl]imidazolinium Tetrafluoroborate (13A): This compound was prepared from **8** (320 mg, 0.89 mmol), NH_4BF_4 (93 mg, 0.89 mmol), and $CH(OEt)_3$ (146 μL, 0.89 mmol) as described in the General Procedure. The mixture was heated at 120 °C for 16 h to give the title compound as a yellow solid (400 mg, 99%); m.p. 80–85 °C. $[a]_D^{22}$ = –116.2 (*c* = 0.37, acetone). ^{1}H NMR (200 MHz, $[D_6]$acetone): δ = 8.27 (s, 1 H), 7.40–7.05 (m, 10 H), 4.92 (d, *J* = 6.3 Hz, 2 H), 4.10–3.40 (m, 10 H) ppm. ^{13}C NMR (50 MHz, $[D_6]$acetone): δ = 160.1, 142.4, 129.4, 128.8, 127.3, 71.4, 67.2, 60.3, 48.4 ppm. IR (KBr): $\tilde{\nu}$ = 3386 m, 1641 vs, 1063 vs, 704 s cm^{-1}. MS (ESI = 0 V): *m*/*z* (%) = 371 (100) $[M]^+$. HRMS (ESI): calcd. for $C_{21}H_{27}N_2O_4^+$ 371.1971; found 371.1980.

1,3-Bis[(1*R*,2*R*)-1,3-dihydroxy-1-phenylprop-2-yl]imidazolinium Tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (13C): This compound was prepared from **13A** (100 mg, 0.22 mmol) and $NaB[C_6H_3(CF_3)_2]_4$ (193 mg, 0.22 mmol) in a mixture of DCM (3 mL) and water (3 mL), as a yellow solid (215 mg, 80%); m.p. 50 °C. $[a]_D^{22}$ = –42.5 (*c* = 4.7, acetone). ^{1}H NMR (200 MHz, $[D_6]$acetone): δ = 8.32 (s, 1 H), 7.70 (br. s, 8 H), 7.55 (br. s, 4 H), 7.40–7.00 (m, 10 H), 5.10–4.90 (m, 2 H), 4.30–3.60 (m, 10 H) ppm. ^{13}C NMR (50 MHz, $[D_6]$acetone): δ = 161.6 (q, *J* = 49.5 Hz), 160.1, 142.4, 135.5, 120.0 (q, *J* = 28.4 Hz), 129.4, 128.9, 127.2, 125.3 (q, *J* = 269.8 Hz), 118.4, 71.6, 67.2, 60.4, 48.5 ppm. IR (KBr): $\tilde{\nu}$ = 1640 w, 1357 s, 1279 vs, 1124 s cm^{-1}. MS (ESI = 0 V): *m*/*z* (%) = 371 (100) $[M]^+$. HRMS (ESI): calcd. for $C_{21}H_{27}N_2O_4^+$ 371.1971; found 371.1974.

(3a*S*,7a*S*)-1,3-Bis[(1*R*,2*R*)-2-hydroxycyclohexyl]-3a,4,5,6,7,7a-hexahydro-3*H*-benzo[*d*]imidazol-1-ium Tetrafluoroborate (14A): This compound was prepared from **9** (310 mg, 1.00 mmol), NH_4BF_4 (113 mg, 1.00 mmol), and $CH(OEt)_3$ (163 μL, 1.00 mmol) as described in the General Procedure, as a yellow solid (380 mg, 93%); m.p. 56 °C. $[a]_D^{22}$ = +7.1 (*c* = 0.1, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.33 (s, 1 H), 4.23 (br. s, 2 H), 3.90–3.30 (m, 6 H), 2.50–0.80 (m, 24 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 158.8, 72.0, 68.9, 63.7, 34.6, 30.3, 28.5, 24.6, 24.0, 23.9 ppm. IR (KBr): $\tilde{\nu}$ = 3528 s, 2940 vs, 2865 s, 1607 vs, 1453 s, 1226 s, 1074 vs, 530 m cm^{-1}. MS (ESI = 0 V): *m*/*z* (%) = 321 (100) $[M]^+$. HRMS (ESI): calcd. for $C_{19}H_{33}N_2O_2^+$ 321.2542; found 321.2540.**Experiment for the Stereodiscrimination of Potassium Mosher's Carboxylate (15):** Mosher's salt (12% *ee*, 0.50 mmol) and the corresponding imidazolinium salt (0.50 mmol, 1 equiv.) were dissolved in $[D_6]$acetone

and the ^{1}H NMR and ^{19}F NMR spectra were recorded at room temp. For chemical shifts and stereodiscrimination see Table 2.

Regeneration of the Salt: Regeneration of imidazolinium salt **10A**. [D_6]Acetone was removed under reduced pressure and the remaining residue was dissolved in $CHCl_3$ (2 mL). The organic phase was washed with water (4 × 3 mL), dried with molecular sieves (3 Å), and concentrated, giving the pure imidazolinium salt **10A**.

General Procedure for Carbene-Catalyzed Et_2Zn Addition to Aldehydes: An imidazolinium salt (0.04 mmol) and *t*BuOK (4.5 mg, 0.04 mmol) were placed in a dry Schlenk flask and dissolved in dry toluene (1 mL). After the mixture had been stirred for 5 min, Et_2Zn (0.5 mL of a 1 M solution in hexane) was added, and after another 5 min, an aldehyde (0.40 mmol) was added. The mixture was stirred at room temp. for 30 h (for differences in reaction times and temperatures see Tables 3 and 4), quenched by the addition of HCl (1 M, 0.5 mL), and extracted with Et_2O (3 × 5 mL). The combined organic phases were dried (Na_2SO_4) and the solvent was removed under reduced pressure to give the crude product, which was purified by flash column chromatography (petroleum ether/ethyl acetate, 9:1) to give the corresponding alcohol.

1-Phenylpropan-1-ol (17): This compound was prepared as a colorless oil from benzaldehyde (**16**, 40 μL, 0.40 mmol) and Et_2Zn (0.50 mL, 1 M solution in hexane) in PhMe (1 mL) and the carbene generated from an imidazolinium salt (0.04 mmol) and *t*BuOK (4.5 mg, 0.04 mmol). For catalysts and yields, see Table 3. Spectral data are consistent with literature values.[38] The enantiomeric ratio was determined by HPLC [OD-H; *i*PrOH/hexane, 10:90; 0.2 mL min^{-1}; $t_1(R)$ = 32.6 min, $t_2(S)$ = 38.8 min].

1-(Naphth-1-yl)propan-1-ol (19): This compound was prepared as a colorless oil from 1-naphthaldehyde (**18**) (56 μL, 0.40 mmol) and Et_2Zn (0.5 mL 1 M solution in hexane) in PhMe (1 mL) and the carbene generated from an imidazolinium carbene precursor (0.04 mmol) and a base. For catalysts, bases, and yields, see Table 4. Spectral data are consistent with literature values.[39] The enantiomeric ratio was determined by HPLC [OD-H; *i*PrOH/hexane, 5:95; 0.4 mL min^{-1}; $t_1(S)$ = 28.4 min, $t_2(R)$ = 55.4 min].

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New enantiopure imidazolinium carbene ligands incorporating two hydroxy groups for Lewis acid-catalyzed diethyl zinc addition to aldehydes

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ABSTRACT

New enantiopure imidazolinium carbene ligands incorporating two hydroxy functions have been synthesized from commercially available chiral amino alcohols and diamines. These ligands in combination with different metallic salts have been investigated in the diethylzinc addition to aldehydes with good yields and enantioselectivity.

1. Introduction

The family of enantiopure *N*-heterocyclic carbenes has emerged as an important class of ligands with many applications in organometallic chemistry[1] and as organocatalysts.[2] In general the carbenes are mainly prepared from the corresponding salts via deprotonation. The latter can also be considered to be part of the class of chiral ionic liquids[3] depending on their melting points. For example, chiral imidazolinium-based ionic liquids have recently been reported.[3b,4] The number of highly selective enantiopure carbene ligands in a few reactions is increased, but remains small compared to the many other applications of chiral phosphine ligands, this makes it desirable to expand upon the library of chiral carbene ligands.[1f]

A limited number of chiral imidazol(in)ium salts incorporating hydroxy groups have been reported. The salts are precursors for bidentate ligands and for example salt **3** has also been used as an ionic liquids.[4a] A very successful bidentate hydroxy-carbene ligand prepared from salt **1** was described by Hoveyda et al.[5] giving up to 96% ee in an asymmetric olefin metathesis and 98% ee in a copper-catalyzed allylic alkylation. Arnold et al. prepared from salt **2** a Cu^{I} complex for the diethylzinc conjugate addition to cyclohexenone, resulting in up to 51% ee.[6] Mauduit et al. used various analogues of salt **4** in the Cu^{II}-catalyzed addition of diethylzinc to cyclohexenone obtaining ees of up to 93% (Fig. 1).[7]

In addition, Alexakis and Mauduit also used analogues of **4** and other chiral imidazolinium salts as carbene precursors in a copper-catalyzed conjugate Grignard addition to 3-substituted cyclohexenones to obtain quaternary chiral centers in up to 96% ee.[8]

Recently, we explored the behavior of a few new imidazolinium salts of type **5** with two hydroxy groups as potential tridentate ligands in the diethyl zinc addition to aldehydes giving up to 66% ee and 67% yield without the addition of an additional metal salt.[4c] In order to explore this group of ligands further, we herein report an expansion of the library of these ligands and a study of the influence of various Lewis acidic metals. In particular oxophilic metals, related to zinc, were explored with these carbene ligands in the diethyl zinc addition[9] to aldehydes in order to prepare optically active secondary alcohols, which are important intermediates in synthesis.

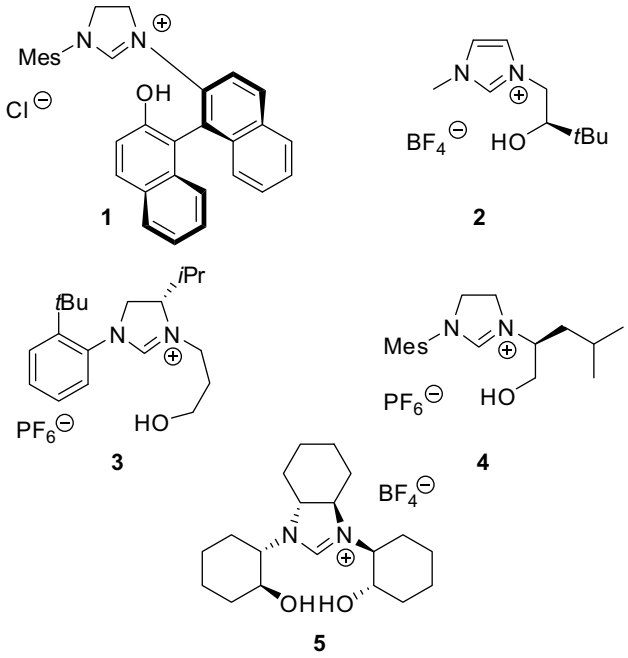

Figure 1. Hydroxy-containing imidazol(in)ium salts.

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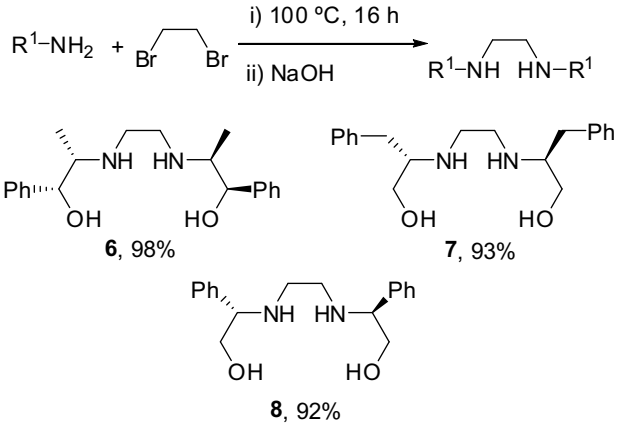
2. Results and discussion

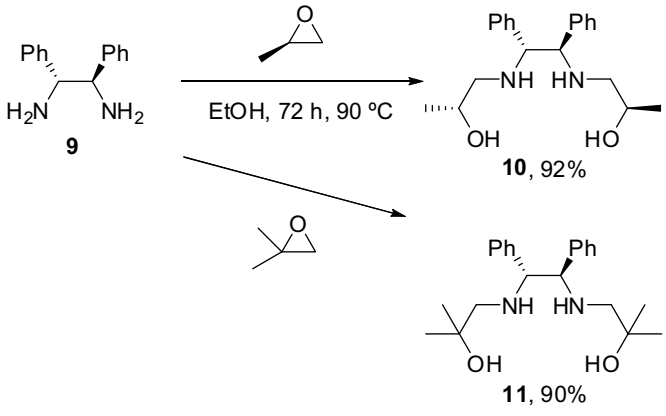
2.1. Preparation of the salts

The synthesis started with the preparation of C_2 symmetric diamines. Two routes were employed for their synthesis. First, diamines bearing hydroxy groups were prepared by simple alkylation of the corresponding amino alcohols with 1,2-dibromoethane via a literature procedure.[10] The reaction was neat and gave excellent yields of the diamines (Scheme 1). The HBr salt of the corresponding diamine was precipitated as a yellow solid in the reaction mixture, which was dissolved in water. After removal of impurities by solvent extraction with chloroform, the aqueous phase was basified with NaOH to obtain pure bis-amino alcohol which was free of acid contents.



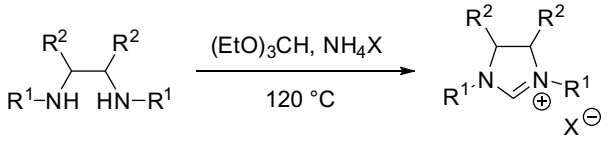
Scheme 1. Alkylation of amino alcohols.

In addition C_2 symmetric amino alcohols were also synthesized by the ring opening of epoxides. Here, chiral diamine **9** was reacted with chiral and achiral epoxides giving rise to β-amino alcohols (Scheme 2). The mixture was refluxed in EtOH for 72 h. The solvent was removed, after which the solid was dissolved in water and acidified to pH 2 with 2 M hydrochloric acid. The aqueous layer was extracted with chloroform which was discarded. The aqueous layer was then basified to pH 11 with 2 M NaOH solution and the product was obtained by extracting the aqueous layer with chloroform. The amino alcohols **10** and **11** were obtained in excellent yields with high purity.



Scheme 2. Ring opening of epoxides.

The salts were then prepared by the direct reaction of the diamines and triethyl orthoformate in the presence of ammonium salts according to a literature procedure.[11] The latter were used as a Brønsted acid source for the activation of the orthoester. These ammonium salts also acted as a source of the anion for the corresponding imidazolinium salts (Scheme 3).

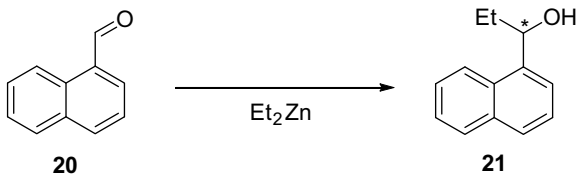


Scheme 3. Synthesis of imidazolinium salts.

Salt **12** has been synthesized from amino alcohol **6** with a yield of 74%.[4c] Salts **13**, **14**, and **15** have the same cation but different anions. Chloride, bromide, and iodide salts were synthesized in order to investigate the influence of harder anions in the diethylzinc addition to aldehydes. Salts **18** and **19** have additional steric information in their backbone, and have been synthesized in excellent yields of 80% and 90%, respectively. The results are summarized in Table 1.

Table 1
Preparation of salts

Entry	Diamine	Cation	Anion	Salt	Yield (%)
1			BF_4^-	**12**	74
2	**6**		Cl^-	**13**	42
3			Br^-	**14**	66
4			I^-	**15**	67
5	**7**		BF_4^-	**16**	57
6	**8**		BF_4^-	**17**	66
7	**10**		BF_4^-	**18**	80
8	**11**		BF_4^-	**19**	90



Scheme 4. Diethylzinc addition to aldehydes.

Table 2
Investigation of the salts: 2.5 mol % $Cu(OTf)_2$, 5 mol % salt, 15 mol % KO*t*Bu, 46 h, rt, toluene

Entry	Salt	Yield (%)	ee (%)	Conf.
1	**12**	42	84	(*R*)
2[a]	**13**	37	44	(*R*)
3	**14**	43	42	(*R*)
4[a]	**15**	31	22	(*R*)
5	**16**	16	0	—
6	**17**	13	0	—
7	**18**	62	12	(*S*)
8	**19**	55	34	(*R*)

[a] 5 mol % $Cu(OTf)_2$, 10 mol % salt, 30 mol % KO*t*Bu.

2.2. Investigation in catalysis

The imidazolinium salts were applied in the diethylzinc addition to 1-naphthaldehyde **20** as shown in Scheme 4 in order to evaluate their efficiency in terms of yield and stereoselectivity.

Therefore, the carbene ligands were employed along with copper(II) triflate (Table 2). It was found that ligand **12** gave the highest ee of 84% with a moderate yield of 42%. Among the other ligands, **18** gave a higher yield of 62% but with a lower ee of 12%. The large influence of the counter-anion on the ee can be attributed to the fact that BF_4, at least in comparison to Cl, Br, and I, is a non-coordinating anion. The halide anions could co-ordinate a metal center and therefore change the catalytic species.

Since the carbene based on salt **12** gave the best results, further optimization was performed with this ligand. Since different metal cations can influence the reaction due to their size, co-ordination sphere, and charge density, several metal salts were investigated in the reaction. The results are summarized in Table 3. $Cu(OTf)_2$ was found to give the highest enantiomeric excess of 84%, but with a moderate yield of 42%. Cupric ions with different counter-anions such as chloride gave 80% ee. However, the yield decreased to 32% indicating the influence of the metallic halide counter-anion, which coordinates to the metal in the catalytic species.

Titanium(IV)chloride gave an ee of 15% while titanium(IV)tetra-isopropoxide resulted in 51% ee. This marked difference can be attributed to the fact that these anions also take part in the transition state formed, depending on their binding strength to the metal cation. Calcium chloride proved to be a better Lewis acid as compared to $MgBr_2$, as can be seen from entries 9 and 10 of Table 3. The results obtained with calcium are remarkable as this metal has not often been used in such a type of catalysis, and is an environmentally friendly cation.

Scandium triflate gave a poor yield of 8% with an ee of 57%. $Ni(acac)_2$ and silver oxide led to an ee of 18% and 10%, respectively. The best yield was 70%, obtained by using zinc triflate with an ee of 63%. Fe^{+2} proved to be superior to Fe^{+3} as the former gave 53% yield with an ee of 63%, while the latter gave 32% yield and 49% ee. It can be seen that the ligand based on salt **12** has a wide range of interaction with several metallic cations.

Table 3
Investigation of salt **12** with different metals: (metal salt:salt **12**:KO*t*Bu) (1:1:3), 46 h, rt, toluene

Entry	Metal salt	Ligand (mol %)	Yield (%)	ee (%)
1	CuI	5	53	80
2	$CuCl_2$	3	32	80
3	$Cu(OTf)_2$	5	42	84
4	$Cu(acac)_2$	10	15	28
5	$FeCl_2$	2	53	63
6	$FeCl_3$	2	32	49
7	$Ti(iPrO)_4$	3	41	51
8	$TiCl_4$	3	34	15
9	$CaCl_2$	5	60	43
10	$MgBr_2$	5	52	25
11	$Sc(OTf)_3$	5	8	57
12	$Ni(acac)_2$	10	52	18
13	Ag_2O	10	14	10
14	$Zn(OTf)_2$	5	70	63
15	$CrCl_3$	5	45	86

Table 4
Investigation of salt **12** with different metals concentrations: (metal salt:salt **12**:KO*t*Bu) (1:1:3), 46 h, rt, toluene

Entry	Metal salt	Ligand (mol %)	Yield (%)	ee (%)
1	CuI	20	21	80
2		10	22	80
3		5	53	84
4		3	55	82
5		1	51	63
6	$Cu(OTf)_2$	10	12	80
7		5	42	84
8		3	44	77
9		1	24	6

In these experiments, three parts of KO*t*Bu were added to one part of the imidazolinium salt in toluene. As shown in Table 5, this was important in order to deprotonate the C2 position and both hydroxyl groups. After 30 min, metallic salt was added and the mixture left to stir for 1 h. Next 1-naphthaldehyde **20** was added, followed by the addition of Et_2Zn (1.1 equiv). The reaction was stirred for 46 h at rt and then quenched with 1 M HCl. Considering the fact that the ligand contains two hard oxygen ligator atoms and one soft carbene moiety, one could explain why these metals (being in the middle of the hard-soft scale) gave the best results. As catalytic active species, a tridentate ligand arrangement can be assumed, as has been reported for tris-oxazoline ligands,[12] which were able to coordinate to a copper center to give a hexaco-ordinated stereo-discriminating complex containing the tridentate ligand, and one water molecule, leaving two co-ordination sites for the substrate.

Table 5
Investigation of base: (metal salt:salt **12**) (1:1), 46 h, rt, toluene

Entry	Base	Base (equiv)	Yield (%)	Ee (%)
1	KO*t*Bu	0.3	42	80
2		0.2	26	80
3		0.1	Traces	—
4	KHMDS	0.3	44	28
5		0.2	31	5
6		0.1	Traces	—

The concentration of the catalyst in the diethyl zinc addition to 1-naphthaldehyde could play a pivotal role on the yield and enantiomeric excess of the product. In order to evaluate the effect of concentration of catalyst, CuI and $Cu(OTf)_2$ were employed as these catalysts prove the best candidates for further investigation as shown in Table 4. When the salt to ligand ratio was 1:1, CuI with 20 mol % of ligand gave 21% yield with 80% ee. Moreover, 10 mol % of ligand gave 22% yield and 80% ee, while 5 mol % of ligand gave 53% yield and 84% ee. A yield of 55% and 82% ee was

found when 3 mol % of the ligand was used. With $Cu(OTf)_2$, 5 mol % of ligand was the best concentration as it gave 42% yield and 84% ee. It is rare but not unknown that lower catalyst loading gives better yield and higher ee.[13] In the present case the drop of ee at lower catalyst loading and therefore lower concentration can be explained by a competitive, ligand-free background reaction. On the other hand, at a higher catalyst loading and therefore higher concentration, it may be possible that an inactive dimer with two copper atoms and two ligands could be formed.

In addition, the influence of the bases KHMDS and KO*t*Bu to generate the carbenes was investigated. The latter gave the best results. KHMDS resulted in 28% ee when 3 equiv was used with a yield of 44% (Table 5, entry 4), while 31% yield was obtained with a low ee of 5%, when 2 equiv of base was applied. KO*t*Bu proved to be the best choice. It can also be concluded from entries 1–3 of Table 5 that 3 equiv of KO*t*Bu is necessary in order to achieve a yield of 42% and an ee of 84%. For all these reactions, $Cu(OTf)_2$ was used and the ligand to salt ratio was 1:1. The need for 3 equiv of KO*t*Bu strongly supports that a tridentate ligand is present in the active catalyst. In addition the enhanced ee resulting in KO*t*Bu can be attributed to the fact that the released *t*BuOH is also participating in the formation of the catalytically active species and could coordinate the metal center. That the alcohol plays such a role is also shown later, when the sterically less hindered ethanol was added, which increased the ee.

In order to further optimize the diethylzinc addition to 1-naphthaldehyde, the reaction was carried out at different temperatures. It was found that by lowering the temperature to 0 °C, the yield decreased markedly to 8% and also a slightly lower ee of 73% was observed (Table 6, entry 5). A further decrease in temperature also decreased the ee to 9% (Table 6, entry 4). For this experiment, *n*-BuLi was used as a base instead of KO*t*Bu, showing again the importance of the presence of *t*BuOH for the enantioselective reaction. When the reaction was carried out at 40 °C, the results were almost similar to those obtained when the reaction was performed at rt (Table 6, entries 1 and 2). Increasing the temperature to 60 °C led to a decrease in yield and in ee of the product, respectively (Table 6, entry 3). The decrease of the ee at higher temperature is obvious since an enantioselective-catalyzed reaction is kinetically controlled. The decrease of the yield and more important the ee at lower temperatures could be explained by the formation of different catalytic copper species and clusters. Similarly, unusual relationships have been observed by Hoveyda[14] and Leighton[15] in the copper-catalyzed enantioselective conjugate addition with chiral phosphine ligands.

Table 6
Investigation of temperature: (metal salt:salt **12**) (1:1), 46 h, rt, toluene

Entry	Salt	*t* (°C)	Yield (%)	ee (%)
1	CuI	rt	53	80
2		40	43	83
3		60	29	56
4[a]	$Cu(OTf)_2$	−50	47	9
5		0	8	73

[a] *n*-BuLi was used as a base.

Table 7
Effect of salt to ligand ratio

Entry	Metal salt	Metal:ligand	Yield (%)	ee (%)
1	$Cu(OTf)_2$	1:1	42	84
2		1:2	76	73
3		2:1	35	11
4		1:4	60	70
5	$Ti(iPrO)_4$	1:1	41	51
6		1:2	54	75

It is known that the salt to ligand ratio can play a crucial role in controlling the outcome of the reaction particularly in terms of yield. In the case of $Cu(OTf)_2$ the yield of the product was maximized to 76% from 42% as the salt to ligand ratio was changed from 1:1 to 1:2. The enantiomeric excess experienced a slight drop from 84% to 73% (Table 7, entries 1 and 2). The reversal of this optimized M:L ratio gave 35% yield and 11% ee (Table 7, entry 3). This can be explained by a ligand-free background reaction. In case of $Ti(iPrO)_4$, when the salt to ligand ratio was changed from 1:1 to 1:2, the yield improved from 41% to 54% and the ee rose from 51% to 75%.

The catalytic system was then examined to determine if a nonlinear effect was present, since the best results were obtained with a metal:ligand ratio of 1:2. Both enantiomers of norephedrine-based imidazolinium salt **12** were mixed in different ratios. The graph obtained shows a slight deviation from linearity, as can be seen from the following graph (Fig. 2). However, taking the error range into consideration no nonlinear effect is present, and the benefit of using a larger amount of ligand is in order to suppress a ligand-free catalyzed background reaction.

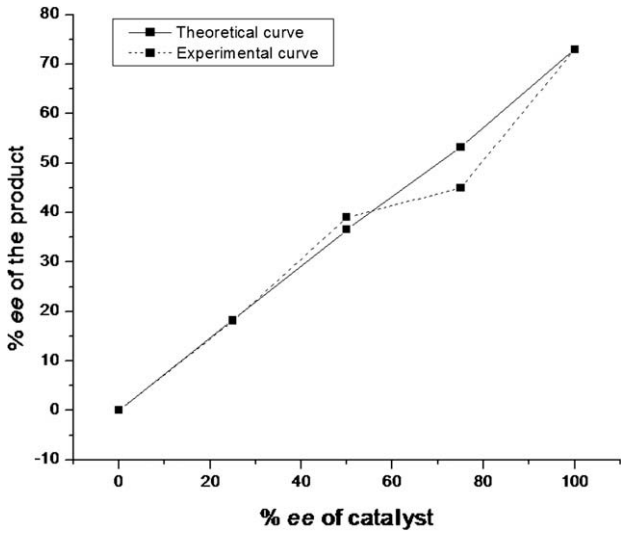


Figure 2. Absence of a nonlinear effect.

The influence of ethanol, as an additive, was also explored. It was seen that addition of ethanol as an additive in the diethylzinc addition to 1-naphthaldehyde showed a marked increase in the ee of the product, that is, 85% as compared with 73% ee, which was obtained without the addition of any additive. However, the yield decreased slightly from 76% to 65%. Furthermore, exploring other solvents revealed that toluene is the best solvent for this system.

In addition, the new bis-amino alcohols *ent*-**10** and **11** were also evaluated as ligands in the diethyl zinc addition to 1-naphthaldehyde. The product was obtained in 77% and 90% yield with an ee of 53 (*S*) and 43% (*R*), respectively.

Finally, different aldehydes were used under the optimized conditions as shown in Table 8. The results were comparable to those of 1-naphthaldehyde.

Table 8
Enantioselective diethylzinc addition to aldehydes[a]

Entry	Aldehyde	Yield (%)	ee (%)	Conf.
1	2-Naphthaldehyde	57	50	(*R*)
2	Benzaldehyde	59	75	(*R*)
3	*p*-Chlorobenzaldehyde	60	78	(*R*)
4	*p*-Methylbenzaldehyde	50	71	(*R*)

[a] $Cu(OTf)_2$:**12**:KO*t*Bu/1:2:3, 46 h, rt, toluene.

Table 9
Chemical shifts δ of Mosher's carboxylate in ppm and $\Delta\delta$ values in Hz (400 MHz ^{1}H NMR, 375 MHz ^{19}F NMR)

Entry	Salt	δ(1H) (*S*)/(*R*)	$\delta(^{19}F)$ (*S*)/(*R*)	$\Delta\delta(^1H)$	$\Delta\delta(^{19}F)$
1	—	3.57/3.57	−71.19/−71.19	0	0
2	**13**	3.56/3.56	−70.75/−70.75	0	0
3	**14**	3.57/3.54	−70.73/−71.04	12	117
4	**15**	3.56/3.53	−70.68/−70.99	12	117
5	**16**	3.56/3.56	−71.06/−71.06	0	0
6	**17**	3.60/3.61	−71.17/−71.17	4	0
7	**18**	3.60/3.60	−70.97/−71.03	0	22
8	**19**	3.62/3.62	−71.07/−71.07	0	0

2.3. Use as a shift reagent

The newly synthesized salts were investigated for their ability to interact with Mosher's carboxylate, by examining the differences in the chemical shifts of the MeO group and the CF_3 group of the two enantiomers of Mosher's carboxylate. In order to assign the signals of the corresponding enantiomers, enantioenriched (12% ee) Mosher's carboxylate was mixed with the chiral imidazolinium salts in a 1:1 ratio. The mixture was dissolved in acetone-d_6 and ^{1}H and ^{19}F NMR spectra were recorded. The results are summarized in Table 9.

Salt **13** showed no splitting in either the ^{1}H or ^{19}F spectra. When the anion was changed from chloride to bromide and iodide, a splitting of 12 Hz in ^{1}H NMR and 117 Hz in ^{19}F NMR was observed in each case (Table 9, entries 3 and 4). Salts **16** and **19** showed no splitting at all, while salt **18** showed a splitting of 22 Hz in ^{19}F NMR and salt **17** displayed a splitting of 4 Hz in ^{1}H NMR.

3. Conclusion

In conclusion, enantiomerically pure imidazolinium-based ligands incorporating two hydroxy groups have been synthesized in moderate to excellent yields by following a simple two-step procedure. The ligands have been employed in the diethylzinc addition to 1-naphthaldehyde, and an ee of up to 84% has been achieved. Moreover, extensive optimization allowed us to understand the behavior of the ligands under different reaction conditions, indicating a tridentate ligand and *t*BuOH coordinating to the metal cation. It was found that copper gave the highest ee in the reaction, which is remarkable since it is normally used for the 1,4 addition of diethyl zinc to unsaturated carbonyl compounds.

4. Experimental

4.1. General experimental

All reactions were carried out in anhydrous solvents under nitrogen. All solvents were dried by standard procedures before being used in the reactions. ^{1}H NMR spectra were acquired with Bruker AC 200F (200 MHz) at ambient temperature. Chemical ^{13}C NMR spectra were recorded at ambient temperature with AC 200F (50 MHz) instruments and ^{19}F NMR spectra were recorded at ambient temperature with a Bruker AMX 400 (378 MHz) instrument. Chemical shifts are reported in ppm relative to tetramethylsilane as an internal standard. Mass spectra (ESI) were recorded with a Hewlett–Packard MS LC/MSD Series 1100 MSD instrument, while high-resolution mass spectra were measured with a Bruker Daltonik Tesla–Fourier Transform-Ion Cyclotron Resonance Mass Spectrometer. Elemental analyses were carried out by the Microanalytical Laboratory of the Institut für Pharmazeutische Chemie der Technische Universität Braunschweig with an Elemental Analyzer Model 1106 from Carlo Erba Instrumentazione. Infrared spectra were recorded with a Bruker Vektor 22 FTIR spectrometer, as KBr pellets in case of solid compounds and as thin films between NaCl plates in cases of oils and liquids. Melting points were taken with a Dr. Tottoli apparatus and are uncorrected.

4.2. Preparation of C_2 symmetric diamines

4.2.1. General procedure for the preparation of diamines by alkylation with dibromoethane

An amino alcohol (1.00 mmol) was added in to a dried flask under nitrogen. Dibromoethane (43 μL, 0.50 mmol) was added via syringe under nitrogen. The reaction mixture was heated at 100 °C for 16 h. The mixture was then cooled to room temperature. After dissolving the solid in water, the aqueous phase was washed with chloroform. The aqueous phase was basified with 2 M NaOH and the diamine was extracted with chloroform (3 × 5 mL). The combined organic fractions were dried (Na_2SO_4) and the solvent was evaporated under reduced pressure to give the bis-amino alcohol.

4.2.2. (−)-(1*R*,1′*R*,2*S*,2′*S*)-2,2′-(Ethane-1,2-diylbis(azanediyl))bis(1-phenylpropan-1-ol) 6

This compound was prepared from (−)-norephedrine (3.00 g, 19.84 mmol) and dibromoethane (0.85 mL, 9.92 mmol), after basification with NaOH as a yellow solid (3.18 g, 98%). Spectroscopic data are consistent with literature values.[16]

4.2.3. (−)-(2*S*,2′*S*)-2,2′-(Ethane-1,2-diylbis(azanediyl))bis(3-phenylpropan-1-ol) 7

This compound was prepared from (−)-(*S*)-2-amino-3-phenyl-1-propanol (0.30 g, 1.98 mmol) and dibromoethane (86.0 μL, 0.99 mmol), after basification with NaOH as a yellow solid (0.30 g, 93%). Spectroscopic data are consistent with literature values.[17]

4.2.4. (+)-(2*S*,2′*S*)-2,2′-(Ethane-1,2-diylbis(azanediyl))bis(2-phenylethanol) 8

This compound was prepared from (+)-(*S*)-phenylglycinol (0.30 g, 2.19 mmol) and dibromoethane (95.0 μL, 1.09 mmol), after basification with NaOH as a yellow oil (0.30 g, 92%). Spectroscopic data are consistent with literature values.[18]

4.2.5. General procedure for the preparation of diamines by ring opening of epoxides

To a stirred solution of chiral 1,2-diphenyl-1,2-ethanediamine (0.21 g, 1.0 mmol) in anhydrous ethanol (5 mL) was added epoxide (3.0 mmol) via a syringe dropwise under an inert atmosphere at room temperature. Upon complete addition, the mixture was heated at reflux for 46 h. After refluxing, the mixture was cooled to room temperature whereupon the solvent was evaporated to give a white solid. The solid was dissolved in water that was acidified to pH 2 with 2 M hydrochloric acid and the aqueous layer extracted with chloroform (3 × 5 mL) which was discarded. The aqueous layer was then basified to pH 11 with 2 M aqueous sodium hydroxide and the aqueous layer was again extracted with chloroform (3 × 5 mL). The combined organic layers were dried over Na_2SO_4, filtered, and evaporated, resulting in a white crystalline solid.

4.2.6. (−)-(*R*,*R*)-1,2-Diphenyl-*N*,*N*′-bis((*R*)-2-hydroxyethyl)-3-methyl)ethylenediamine 10

This amino alcohol was synthesized from (+)-(1*R*,2*R*)-1,2-diphenyl-1,2-ethanediamine (0.20 g, 0.94 mmol) and (+)-(*R*)-propylene oxide (0.20 mL, 2.83 mmol) by following the general procedure as a white crystalline solid (0.287 g, 93%). mp 119 °C. $[\alpha]_D^{22} = -30$

(*c* 1.0, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 7.07–6.94 (m, 10H), 3.80–3.70 (m, 2H), 3.63 (s, 2H) 2.43–2.16 (m, 4H), 0.98 (d, J = 5.4 Hz, 6H) ^{13}C NMR (50 MHz, $CDCl_3$) δ 140.7, 128.0, 127.7, 127.0, 68.3, 65.9, 54.3, 20.5. IR (KBr): 3303, 2961, 2909, 1646, 1454, 1126, 1051, 864, 772, 700, 625, 575 cm^{-1}. MS (ESI = 0 V): m/z = 351 [M+Na]. HRMS (ESI): calcd for $C_{21}H_{29}N_2O_2$ [M+H]: 329.2229; found 329.2229.

4.2.7. (+)-(*R,R*)-1,2-Diphenyl-*N,N′*-bis(2-hydroxy-2-methylpropyl)ethylenediamine 11

This amino alcohol was synthesized from (+)-(1*R*,2*R*)-1,2-diphenyl-1,2-ethanediamine (0.10 g, 0.47 mmol) and isobutylene oxide (0.13 mL, 1.41 mmol) by following the general procedure as a white crystalline solid (0.148 g, 90%). mp 123 °C. $[\alpha]_D^{22} = +13$ (*c* 0.5, MeOH); ^1H NMR (200 MHz, $CDCl_3$) δ 7.26–6.98 (m, 10H), 3.69 (s, 2H) 2.36 (s, 6H), 1.17 (s, 6H), 1.13 (s, 6H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 141.0, 128.0, 127.6, 127.0, 69.9, 69.6, 58.1, 27.4, 27.3. IR (KBr): 3302, 2962, 2907, 1455, 1405, 1164, 1127, 896, 845, 764, 699, 580 cm^{-1}. MS (ESI = 0 V): m/z (%) = 379 (70%) [M+Na], 357 (60) [M+H]. HRMS (ESI): calcd for $C_{21}H_{33}N_2O_2$ [M+H]: 357.2542; found 357.2542.

4.2.8. General procedure for preparation of imidazolinium salts

A bis-amino alcohol (1.00 mmol) was placed in a flask, and the counteranion source (typically NH_4BF_4, 1.00 mmol) and triethyl orthoformate (148 mg, 165 μL, 1.00 mmol) was added. The reaction vessel was flushed with nitrogen and sealed, and the mixture was heated to 120 °C for 5 h. After cooling, the mixture was dried under vacuum, in order to remove ethanol, formed during the reaction, to give the crude salt in high purity.

4.2.9. (−)-1,3-Bis[(1*S*,2*R*)-2-hydroxy-1-methyl-2-phenylethyl]imidazolinium tetrafluoroborate 12

This compound was prepared from **6** (500 mg, 1.52 mmol), NH_4BF_4 (156 mg, 1.52 mmol), and $CH(OEt)_3$ (250 μL, 1.52 mmol). The reaction mixture was heated to 120 °C in a sealed vessel for 5 h. After removing the ethanol, the crude was washed with hexane, diethyl ether, and dichloromethane giving the title compound as a white solid (481 mg, 74%). Spectroscopic data are consistent with literature values.[4c]

4.2.10. (−)-3-Bis-[(1*S*,2*R*)-2-hydroxy-1-methyl-2-phenyl-ethyl]-imidazolinium chloride 13

This compound was prepared from **6** (300 mg, 0.91 mmol), NH_4Cl (48.8 mg, 0.91 mmol), and $CH(OEt)_3$ (148 μL, 0.91 mmol). The reaction mixture was heated to 120 °C in a sealed vessel for 16 h. After removal of the solvent, the crude was washed with hexane, diethyl ether, and chloroform giving the title compound as a white crystalline solid (143 mg, 42%); mp 199 °C. $[\alpha]_D^{22} = -16$ (*c* 0.4, MeOH); ^1H NMR (200 MHz, CD_3OD) δ 7.90 (s, 1H), 7.17–7.08 (m, 10H), 4.61 (d, J = 4.4 Hz, 2H), 3.71–3.59 (m, 6H), 1.07 (d, J = 7.0 Hz, 6H). ^{13}C NMR (50 MHz, CD_3OD) δ 156.3, 140.6, 128.1, 127.6, 126.0, 73.7, 59.4, 47.0, 11.9; IR (KBr) 3298, 3223, 1246, 1148, 1050, 995, 744, 698 cm^{-1}. MS (ESI = 0 V): m/z (%) = 339 [M]. HRMS (ESI): calcd for $C_{21}H_{27}N_2O_2^+$ 339.2073; found 339.2073.

4.2.11. (−)-1,3-Bis-[(1*S*,2*R*)-2-hydroxy-1-methyl-2-phenyl-ethyl]-imidazolinium bromide 14

This compound was prepared from **6** (100 mg, 0.30 mmol), NH_4Br (32.2 mg, 0.33 mmol), and $CH(OEt)_3$ (56 μL, 0.34 mmol). The reaction mixture was heated to 120 °C in a sealed vessel for 12 h. After the removal of solvent, the crude was washed with hexane and diethyl ether giving the title compound as a yellow crystalline solid (84 mg, 66%); mp 148 °C. $[\alpha]_D^{22} = -17$ (*c* 1.0, MeOH); ^1H NMR (200 MHz, $(CD_3)_2CO$) δ 8.51 (s, 1H), 7.28–7.04 (m, 10H), 5.68 (d, J = 4.0 Hz, 2H), 5.10 (br s, 2H) 4.09–3.86 (m, 6H), 0.85 (d, J = 7.0 Hz, 6H). ^{13}C NMR (50 MHz, $(CD_3)_2CO$) δ 157.2, 142.3, 128.9, 127.7, 126.8, 72.3, 60.3, 48.8, 11.1. IR (KBr) 3344, 1647, 1266, 1151, 753, 704 cm^{-1}: MS (ESI = 0 V): m/z (%) = 339 [M]. HRMS (ESI): calcd for $C_{21}H_{27}N_2O_2^+$ 339.2073; found 339.2070.

4.2.12. (−)-3-Bis-[(1*S*,2*R*)-2-hydroxy-1-methyl-2-phenyl-ethyl]-imidazolinium iodide 15

This compound was prepared from **6** (200 mg, 0.61 mmol), NH_4I (88.3 mg, 0.61 mmol), and $CH(OEt)_3$ (100 μL, 0.61 mmol). The reaction mixture was heated to 120 °C in a sealed vessel for 5 h. After the removal of the solvent, the crude was washed with hexane and diethyl ether giving the title compound as a white crystalline solid (189 mg, 67%). Compound **15** was recrystallized in acetone for X-ray crystallography. mp 184 °C. $[\alpha]_D^{22} = -4$ (*c* 0.3, MeOH); ^1H NMR (200 MHz, CD_3OD) δ 7.90 (s, 1H), 7.16–7.08 (m, 10H), 4.61 (s, 2H), 3.72–3.60 (m, 6H), 1.00 (d, J = 7.0 Hz, 6H). ^{13}C NMR (50 MHz, CD_3OD) δ 157.8, 142.1, 129.6, 129.1, 127.5, 75.2, 60.9, 47.2, 13.5. IR (KBr): 3438, 3236, 1650, 1496, 1262, 1138, 1029, 1016, 753, 704 cm^{-1}. MS (ESI = 0 V): m/z = 339 [M]. HRMS (ESI): calcd for $C_{21}H_{27}N_2O_2^+$ 339.2073; found 339.2072.

4.2.13. (−)-1,3-Bis[(*S*)-1-(hydroxymethyl)-2-methylbenzyl]-imidazolinium tetrafluoroborate 16

This compound was prepared from **7** (200 mg, 0.61 mmol), NH_4BF_4 (68.6 mg, 0.67 mmol), and $CH(OEt)_3$ (109 μL, 0.67 mmol). The reaction mixture was heated to 120 °C in a sealed vessel for 5 h. After removal of the solvent, the crude was washed with hexane and diethyl ether giving the title yellow gummy compound (147 mg, 57%). $[\alpha]_D^{22} = -71$ (*c* 1.0, $CHCl_3$); ^1H NMR (200 MHz, $(CD_3)_2CO$) δ 8.16 (s, 1H), 7.20–7.14 (m, 10H), 3.57–3.95 (m, 12H), 2.84 (m, 4H). ^{13}C NMR (50 MHz, $(CD_3)_2CO$) δ 158.6, 137.9, 129.9, 129.6, 127.7, 62.8, 61.3, 46.9, 35.6. IR (NaCl): 3054, 2987, 1422, 1265, 896, 739 cm^{-1}. MS (ESI = 0 V): m/z = 339 [M]. HRMS (ESI): calcd for $C_{21}H_{27}N_2O_2^+$ 339.2073; found 339.2075.

4.2.14. (+)-1,3-Bis[(*S*)-1-(hydroxymethyl)-2-methylphenyl]-imidazolinium tetrafluoroborate 17

This compound was prepared from **8** (100 mg, 0.33 mmol), NH_4BF_4 (53.8 mg, 0.49 mmol), and $CH(OEt)_3$ (83 μL, 0.49 mmol). The reaction mixture was heated to 120 °C in a sealed vessel for 16 h. After the removal of the solvent, the crude was washed with hexane and diethyl ether giving a yellow oil (87 mg, 66%). $[\alpha]_D^{22} = +65$ (*c* 0.65, MeOH); ^1H NMR (200 MHz, $(CD_3)_2CO$) δ 8.74 (s, 1H), 7.33–7.24 (m, 10H), 4.97–4.91 (m, 2H), 4.54 (s, br, 2H), 3.90–3.82 (m, 8H). ^{13}C NMR (50 MHz, $(CD_3)_2CO$) δ 158.5, 135.5, 129.9, 129.7, 128.7, 64.9, 62.1, 47.4. IR (NaCl): 3054, 2987, 1422, 1265, 896, 739 cm^{-1}. MS (ESI = 0 V): m/z = 311 [M]. HRMS (ESI): calcd for $C_{19}H_{23}N_2O_2^+$ 311.1760; found 311.1761.

4.2.15. (+)-(4*R*,5*R*)-Diphenyl-1,3-bis((*R*)-2-hydroxyethyl)-3-methyl)-imidazolinium tetrafluoroborate 18

This compound was prepared from **10** (104 mg, 0.32 mmol), NH_4BF_4 (35.8 mg, 0.35 mmol), and $CH(OEt)_3$ (58 μL, 0.35 mmol). The reaction mixture was heated to 120 °C in a sealed vessel for 5 h. After the removal of solvent, the crude was washed with hexane and diethyl ether giving the white crystalline compound (143 mg, 80%). mp 118 °C. $[\alpha]_D^{22} = -51$ (*c* 1.2, $CHCl_3$); ^1H NMR (200 MHz, $(CD_3)_2CO$) δ 8.72 (s, 1H), 7.44–7.33 (m, 10H), 4.48 (d, J = 5.6Hz, 2H), 4.01 (s, br, 2H), 3.52–3.06 (m, 4H), 1.03 (d, J = 6.2 Hz, 6H). ^{13}C NMR (50 MHz, $(CD_3)_2CO$) δ 160.1, 136.9, 130.4, 128.6, 73.4, 63.2, 53.5, 20.9. IR (KBr): 3346, 2971, 1640, 1458, 1211, 1083, 763, 702, 625, 522 cm^{-1}. MS (ESI = 0 V): m/z = 339 [M]. HRMS (ESI): calcd for $C_{21}H_{27}N_2O_2^+$ 339.2073; found 339.2064.

4.2.16. (+)-(4*R*,5*R*)-Diphenyl-1,3-bis(2-hydroxy-2-methylpropyl)-imidazolinium tetrafluoroborate 19

This compound was prepared from **11** (150 mg, 0.42 mmol), NH_4BF_4 (47.5 mg, 0.46 mmol), and $CH(OEt)_3$ (78 μL, 0.46 mmol). The reaction mixture was heated to 120 °C in a sealed vessel for 12 h. After removal of the solvent, the crude was washed with hexane and diethyl ether to give a white crystalline compound (170 mg, 90%). mp 108 °C. $[\alpha]_D^{22} = +150$ (*c* 1.1, MeOH); ^{1}H NMR (200 MHz, $(CD_3)_2CO$) δ 8.84 (s, 1H), 7.44–7.33 (m, 10H), 5.43 (s, 2H), 3.68–3.61 (m, 4H) 3.14 (s, 1H), 3.07 (s, 1H) 1.18 (s, 6H), 1.10 (s, 6H) ^{13}C NMR (50 MHz, $(CD_3)_2CO$) δ 157.2, 142.3, 128.9, 127.7, 126.8, 72.3, 60.3, 48.8, 11.1. IR (KBr): 3355, 2976, 1638, 1457, 1379, 1159, 1061, 763, 702, 625 cm^{-1}. MS (ESI = 0 V): *m*/*z* = 367 [M]. HRMS (ESI): calcd for $C_{23}H_{31}N_2O_2^+$ 367.2386; found 367.2383.

4.2.17. General procedure for Et_2Zn addition to aldehydes

An imidazolinium salt (0.017 mmol) and KO*t*Bu (6.1 mg, 0.051 mmol) were placed in a dry Schlenk flask and dry toluene (1 mL) was added. After stirring the mixture for 30 min, $Cu(OTf)_2$ (3.2 mg, 0.009) mmol) was added and left to stir for 1 h. Aldehyde (0.35 mmol) was added and the mixture was stirred for 5 min. Then Et_2Zn (0.5 mL of a 1 0 M solution in hexane) was added dropwise. The mixture was stirred at rt for 46 h, quenched by the addition of 1 M HCl (1 mL), and extracted with Et_2O (3 × 5 mL). The combined organic phases were dried over Na_2SO_4 and the solvent was removed under reduced pressure to give the crude product, which was purified by flash column chromatography (petroleum ether/ethyl acetate, 9:1) to give the corresponding alcohol **21**.

4.2.18. (*R*)-1-(1-Naphthyl)-propan-1-ol 21

$[\alpha]_D^{22} = +35$ (*c* 0.30, $CHCl_3$). For catalysts, bases, yields, and ee see Tables 1–7. Spectroscopic data were consistent with literature values.[4] 73% ee (*R*) by HPLC analysis [OD–H; *i*PrOH/hexane, 5:95; 0.4 mL min^{-1}; $t_1(S)$ = 35.7 min, $t_2(R)$ = 67.6 min].

4.2.19. (*R*)-1-(2-Naphthyl)-propan-1-ol

Yield = 57%; $[\alpha]_D^{22} = +29$ (*c* 0.50, $CHCl_3$). 50% ee (*R*) by HPLC analysis [OD-H; *i*PrOH/hexane, 10:90; 1.0 mL min^{-1}; $t_1(S)$ = 10.0 min, $t_2(R)$ = 11.0 min]. Spectroscopic data were consistent with literature values.[4]

4.2.20. (*R*)-1-Phenyl-1-propanol

Yield = 39%; $[\alpha]_D^{22} = +36$ (*c* 0.50, $CHCl_3$). 75% ee (*R*) by HPLC analysis [OD-H; *i*PrOH/hexane, 5:95; 1.0 mL min^{-1}; $t_1(R)$ = 8.0 min, $t_2(S)$ = 9.0 min]. Spectroscopic data were consistent with literature values.[4]

4.2.21. (*R*)-1-(4-Chlorophenyl)-1-propanol

Yield = 60%; $[\alpha]_D^{22} = +28$ (*c* 1.33, $CHCl_3$). 78% ee (*R*) by HPLC analysis [OD-H; *i*PrOH/hexane, 2.5:97.5; 1.0 mL min^{-1}; $t_1(S)$ = 11.8 min, $t_2(R)$ = 12.5 min]. Spectroscopic data were consistent with literature values.[4]

4.2.22. (*R*)-1-(4-Methylphenyl)-1-propanol

Yield = 50%; $[\alpha]_D^{22} = +32$ (*c* 1.0, $CHCl_3$). 71% ee (*R*) by HPLC analysis [OD–H; *i*PrOH/hexane, 0.1:99.9; 1.0 mL min^{-1}; $t_1(R)$ = 67.7 min, $t_2(S)$ = 85.0 min]. Spectroscopic data were consistent with literature values.[4]

4.3. NMR Experiments with Mosher's acid salt

4.3.1. Preparation of racemic potassium Mosher's carboxylate

Racemic Mosher's acid (302 mg, 1.29 mmol) was dissolved in water (1 mL) and a solution of KOH (72 mg, 1.29 mmol) in water (3 mL) was added. The mixture was stirred at rt for 15 min and water was removed under reduced pressure. The remaining solid was further dried under high vacuum to give the potassium Mosher's carboxylate salt as a white solid (351 mg, quant).

4.3.2. NMR experiment with the racemic Mosher's acid salt

The Mosher's acid salt (1 mmol) and the corresponding imidazolinium salt (1 mmol) were dissolved in acetone-d_6 and the ^{1}H NMR and ^{19}F NMR spectra were recorded at rt. For results see Table 8.

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New enantiopure NHCs derived from camphor†

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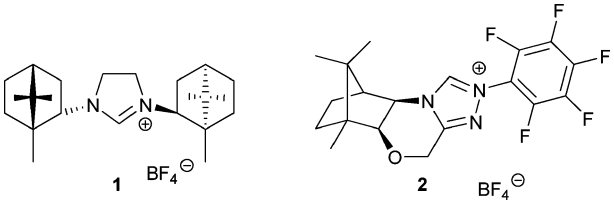
A new class of enantiopure carbene precursors based on cheap camphor has been developed, and a restricted rotation of one N-substituent due to the C-10 methyl group of the camphor skeleton has been found; *in situ* prepared corresponding carbenes revealed the same behaviour.

NHCs (N-heterocyclic carbenes) have recently emerged as a new important family of ligands in various applications in organometallic chemistry and as organocatalysts.[1] As the next step several enantiopure NHC precursors have been prepared and applied in many transformations.[1,2] However, although camphor is a cheap desirable starting material from the chiral pool, only a few carbene precursors such as **1**[2a] or **2**[2b] have been prepared and successfully used so far as ligands or as organocatalysts in asymmetric catalysis.



C_1 symmetric chiral camphor-based carbene precursors of type **5** have not been reported so far (Scheme 1). The NCN unit would be embedded in a rigid bicyclic system being part of a six and seven-membered ring. Hence, the corresponding carbene possesses a higher basicity than carbenes with imidazolium and imidazolinium moieties.[3] In addition, the free rotation of a substituent next to the C-10 methyl group of the camphor skeleton could be limited due to steric hindrance, which could provide an asymmetric differentiation in a catalytic reaction step. The diamine **3** can be prepared readily *via* a Schmidt reaction from (+)-camphoric acid,[4] a cheap chiral building block derived from camphor.

First, the desired carbene precursors **5a–c** were prepared as shown in Scheme 1 *via* standard transformations from diamine **3** and $MesCH_2Cl$, benzaldehyde or anthracene-9-carbaldehyde. In addition, salt **7** was prepared according to Scheme 1 by applying only 1 equiv. of 2,4,6-trimethyl benzyl chloride and amine **6** was isolated in 69% yield due to the larger steric hindrance on one of the amine function in **3**.

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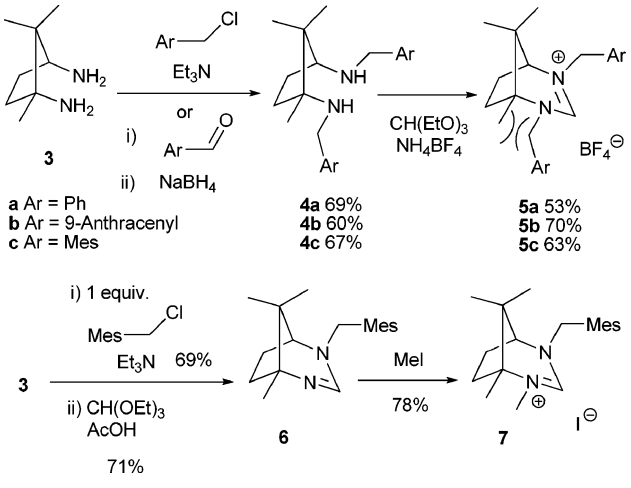
† Electronic supplementary information (ESI) available: Full experimental procedures, spectra and HPLC runs. See DOI: 10.1039/b911476a

A restricted rotation in salts **5b** and **5c** was shown to be present by the ^{1}H-NMR signal of the C(2)–H bond. Compounds **5b** and **5c** are shifted upfield to 4.79 and 5.89 ppm, respectively. On the other hand the signals of salts **5a** and **7** are at 8.47 and 8.94 ppm. The large upfield shift of the protons of **5b** and **5c** is due to the fact that they are in close proximity to the middle of the arene rings next to the C-10 methyl group of the camphor skeleton. Unfortunately it was not possible to acquire an X-ray structure of the salts to see the conformation in the solid state.

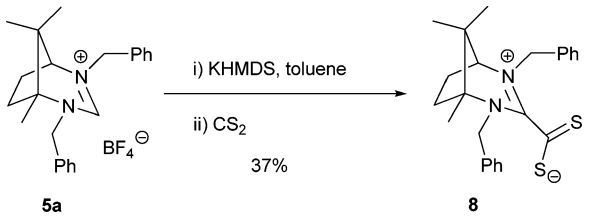
In order to show that the carbenes are formed from the salts, **5a** was treated with KHMDS in toluene for 30 min as an example. Thereafter, the carbene was trapped by the addition of CS_2 and after 10 min the product **8** was isolated in 37% yield as a red solid (Scheme 2).

Due to the absence of the C(2)-proton in the corresponding carbenes, it would be difficult to verify the suggested conformation of the carbenes by NMR measurements as it was done for the precursor salts. Hence, it was decided to support this assumption by using the carbenes as Lewis base catalysts in a formal [2 + 2] reaction of ketenes and aldehydes. This enantioselective reaction[5] is a straightforward way to obtain β-lactones from aldehydes and ketenes (Scheme 3). Optically active β-lactones are important synthons.[6] Recently, Ye *et al.*[5j] applied an enantiopure triazolium salt based carbene in the [2 + 2] reaction of electron deficient 2-oxoaldehydes with alkyl(aryl)ketenes and diarylketenes, while Fu and Wilson catalyzed the [2 + 2] reaction of benzaldehydes with dialkylketenes with an enantiopure planar DMAP ferrocene derivative.[5f]

In such a reaction with carbenes derived from **5a–c** the following mechanism would be reasonable as shown in



Scheme 1 Preparation of NHC precursors.



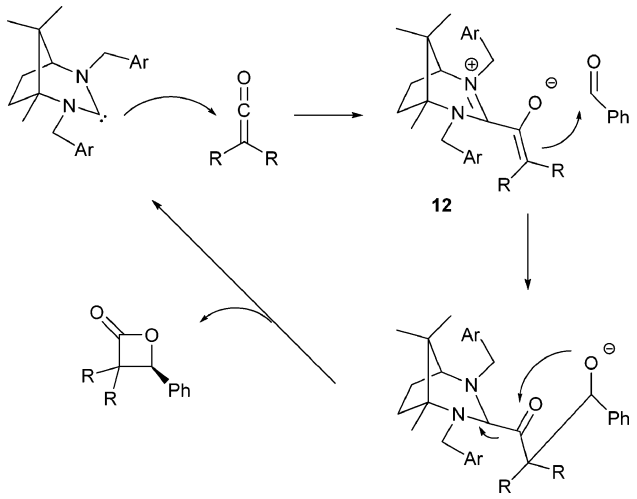
Scheme 2 Trapping the carbene with CS_2.

Scheme 3 [2 + 2] Reaction of ketenes with aldehydes.

Scheme 4. The carbene attacks the ketene. Since the ketene is shielded from one side, the aldehyde can only approach from the side opposite of the C-10 methyl group of the camphor skeleton. After the new bond is formed the carbene is released with the formation of an (*S*)-β-lactone. It is reasonable to assume that in intermediate **12** the NCN unit and the enolate are not in one plane but perpendicular to each other due to steric hindrance in analogy to the CS_2 adduct **8** and other literature reported analogues.[7]

First, the reaction of ketene **9** (R^1,R^2 = –$(CH_2)_6$–) and benzaldehyde was chosen in order to screen the different carbenes and to optimize conditions (Scheme 3). The results are summarized in Table 1. The carbenes were generated from the different salts by treating them with KHMDS at −60 °C and warming up the solution to rt to give a yellow solution. Thereafter, the reaction was cooled down to −20 °C and benzaldehyde was added followed by the addition of 1.5 equiv. of ketene.

With salt **5b** and KHMDS in dry toluene the desired product was formed in 72% yield and 51% ee (Table 1, Entry 1). By lowering the temperature it was possible to increase the ee to 92%, while the yield remained the same (Table 1, Entries 2 and 3). The reaction was repeated under the same conditions with the other salts. Salt **5c** gave nearly the same yield as **5b**, but



Scheme 4 Possible mechanism.

Table 1 Different NHC salts in the [2 + 2] reaction with benzaldehyde[a]

Entry	Salt	T/°C	Yield (%)	ee (%)
1	**5b**	−20	72	51
2	**5b**	−40	70	86
3	**5b**	−60	75	92
4	**5c**	−60	69	73
5	**5a**	−60	32	19
6	**7**	−60	21	0

[a] With ketene **9**, benzaldehyde, 10 mol% salt and 8 mol% KHMDS in toluene.

with a lower ee of 73% (Table 1, Entry 4). The less hindered salt **5a** resulted in a yield of 32% and an ee of 19% (Table 1, Entry 5). Finally, salt **7** gave, as expected, racemic product in 21% yield (Table 1, Entry 8). In all cases the (*S*)-β-lactone was the major enantiomer.

With the optimized conditions in hand, different ketenes and aldehydes were applied in the reaction with salt **5b** as catalyst precursor as shown in Scheme 3. The results are summarized in Table 2. The reactions were carried out at −78 °C, although it did not have an influence on the result compared to −60 °C (Table 2, Entry 1). Different aldehydes were used with ketene **9** and it was found that electron deficient and electron rich aldehydes gave up to 91% ee (Table 2, Entries 2–5). Next, a solution of cyclopentylmethyl ketene in toluene[8] with benzaldehyde gave the product in 99% yield. Both diastereomers had nearly the same ee of 80% (Table 2, Entry 6).

In one example the reaction was worked up with a 2% aq. solution of NH_4BF_4 and the regenerated salt **5b** could be recovered during column chromatography in 81% yield by changing the mobile phase after the isolation of the product to a 5% methanol–CH_2Cl_2 mobile phase.

In summary, a novel class of enantiopure carbene precursors based on camphoric acid has been prepared. The generated highly nucleophilic carbenes were able to catalyze a formal [2 + 2] reaction of ketenes with aldehydes. In these new carbenes the small C-10 methyl group is responsible for the chirality transfer. Good yield and significant ee were achieved, which was for product **11** (Table 2, Entry 1) an increase of 10% compared to the so far best reported ee in the literature.[5f] Current work within the group is exploring these new carbenes and further analogues as ligands in metal catalyzed reactions.

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Table 2 Salt **5b** with different ketenes and aldehydes[a]

Entry	Ketene	Aldehyde	Yield (%)	ee (%)
1	–$(CH_2)_6$–	Ph	76	92
2	–$(CH_2)_6$–	4-F-C_6H_4	72	91
3	–$(CH_2)_6$–	4-Me-C_6H_4	82	91
4	–$(CH_2)_6$–	2-Me-C_6H_4	73	80
5	–$(CH_2)_6$–	4-Cl-C_6H_4	80	81
6[b]	C_5H_9, Me	Ph	99	82, 79

[a] 10 mol% salt **5b** and 8 mol% KHMDS at −78 °C. [b] Ketene prepared according to ref. 8 as a 0.24 M solution in toluene, *trans* : *cis* ratio 1 : 2.

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8 A solution of 0.35 M ketene in toluene was prepared by stirring 1 equiv. of 2-cyclopentylpropanoyl chloride and 1 equiv. DABCO in toluene at 80 °C for 3 h. After cooling down to rt, the ketene was condensed with the toluene under high vacuum in a Schlenk tube cooled with liquid nitrogen. The concentration was calculated *via* the addition of *n*-$PrNH_2$ to a solution.

Hindered Brønsted bases as Lewis base catalysts

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KHMDS and KO*t*Bu are well established as strong, hindered, non-nucleophilic Brønsted bases. However, in the present work these bases are applied as highly active Lewis base catalysts for the formal [2+2] cycloaddition of ketenes with aldehydes and imines.

Introduction

Alkali metal hexamethyldisilazanes are well known as non-nucleophilic hindered Brønsted bases and are extensively used in synthesis.[1] HMDS has a pK_a of 26 and *N*,*N*-diisopropylamine a pK_a of 36 in THF. HO*t*Bu has a pK_a of 29.4 in DMSO.[2] The lower pK_a of HMDS can be explained by α-silyl stabilization.[3] However, a few examples where these bases act as nucleophiles are also known. Despite its lower basicity and the more pronounced sterical screening of the nitrogen atom of MHMDS compared to LDA, more examples[4] of the HMDS anion acting as a nucleophile are known than for LDA.[5] Moreover, KO*t*Bu may also act as a nucleophile.[6]

The Staudinger cycloaddition[7] as well as the formal [2+2] cycloaddition of aldehydes and ketenes, the Wynberg reaction,[8] are established methods to obtain β-lactams and β-lactones,[9] which are important compounds due to their biological activity and utility in synthesis.[10] The reactions are often promoted by Lewis base catalysts. These catalysts are normally weak Brønsted bases.

Here we report that the hindered strong base NaHMDS/KHMDS is an efficient Lewis base catalyst for the Staudinger reaction of disubstituted ketenes and imines with a *para*-nosyl group.[11] In addition hindered Brønsted bases are also active catalysts for the cycloaddition of ketenes with aldehydes and reactions were conducted to exclude some possible mechanistic pathways.

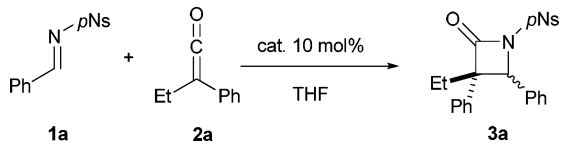
Results and discussion

Several Lewis bases were screened for their nucleophilic capacity to catalyze the Staudinger cycloaddition of imine **1a** with a *para*-nosyl group and phenylethyl ketene **2a** (Scheme 1). Along with strong amine bases, alkali metal amides were also tested under different reaction conditions as shown in Table 1. Due to their nucleophilic nature, the best results were observed in the cases when amide catalysts were applied. Furthermore, the character of the alkali metal had an influence on the reaction. NaHMDS and KHMDS resulted in total conversion at −78 °C in less than 5 min and 10 min respectively (Table 1, entries 1 and 5), however LiHMDS gave just a moderate yield of 28% in 3 h (Table 1, entry 6). LDA catalyzed the reaction in a good yield of 77% but the reaction time increased to 1.5 h, and a decrease in the diastereoselectivity was observed (Table 1, entry 8). This can be attributed to the lower nucleophilicity of the lithium amides, due to the stronger covalent bond character between the lithium and nitrogen.

Table 1 Staudinger reaction of **1a** and **2a** catalyzed by 10 mol% of catalysts at −78 °C in THF

entry	catalyst	T [min]	yield [%][a]	*trans*:*cis*
1	KHMDS	10 min	85	20:80
2[b]		5 min	99	33:66
3[b,c]		1 h	99	20:80
4[c]		24 h	0	—
5	NaHMDS	<5 min	99	20:80
6	LiHMDS	3 h	28	20:80
7	HMDS	24 h	0	—
8	LDA	1.5 h	77	28:72
9[d]	NaOTMS	20 min	48	37:63
10	DMAP	3.5 h	92	55:45
11	Et_3N	24 h	17	50:50
12	DABCO	24 h	44	50:50
13[b]	DBU	24 h	*traces*	—
14[b]	—	24 h	0	—

[a] Yields of isolated **3a**. [b] Reaction performed at rt. [c] Reaction performed in toluene. [d] Reaction was stopped by quenching with $NH_4Cl_{(aq)}$ at −78 °C.



1a **2a** **3a**

Scheme 1 Staudinger reaction catalyzed by different Lewis bases.

When toluene was used as a solvent instead of THF only traces of the product were obtained at −78 °C with KHMDS. This can be mainly explained by the poor solubility of the imines.[12] At room temperature the reaction proceeded in toluene with quantitative yield, and the diastereomeric ratio of the product was found to be similar to that obtained at −78 °C in THF (Table 1, entry 3). The reaction performed in THF at room temperature (Table 1, entry 2) resulted in a decrease in the diastereomeric ratio.

As shown in Scheme 2, it is known that NaHMDS reacts with aldehydes to form TMS-protected imines with liberation of NaOTMS. This reaction is much faster with LiHMDS and can be carried out at −40 °C, but it is much slower with KHMDS.[4i] Since alkoxides have not so far been used as Lewis base catalysts in [2+2] cycloadditions, the Staudinger reaction was repeated with NaOTMS as a potential catalyst (Table 1, entry 9). The reaction was stopped after 20 min in order to compare

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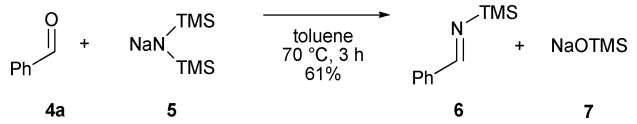
Table 2 Staudinger reaction with different imines **1** and ketenes **2**, catalyzed by 10 mol% MHMDS

entry	imine	ketene	base	T [min]	yield [%][a]	**3**[b] (*trans:cis*)
1	**1a** Ph	**2a** R^1 = Et R^2 = Ph	NaHMDS	< 5	99	**3a** (20:80)
2	**1b** 2-Cl-C_6H_4	**2a**	KHMDS	< 3	99	**3b** (12:88)
3	**1c** 2-Thiophenyl	**2a**	KHMDS	15	68	**3c** (43:57)
4	**1d** 1-Naphthyl	**2a**	KHMDS	90	89	**3d** (14:86)
5	**1e** 2-Naphthyl	**2a**	NaHMDS	10	98	**3e** (45:55)
6	**1f** 4-CH_3-C_6H_4	**2a**	NaHMDS	< 10	87	**3f** (33:67)
7	**1g** 4-Cl-C_6H_4	**2a**	NaHMDS	< 5	92	**3g** (26:74)
8	**1h** 4-CF_3-C_6H_4	**2a**	KHMDS	10	99	**3h** (43:57)
9	**1i** 4-NC-C_6H_4	**2a**	NaHMDS	15	99	**3i** (36:64)
10	**1j** 4-F-C_6H_4	**2a**	KHMDS	10	98	**3j** (25:75)
11	**1k** 3,4-$(MeO)_2$-C_6H_3	**2a**	NaHMDS	120	88	**3k** (22:78)
12	**1a** Ph	**2b** R^1 = Me R^2 =Ph	NaHMDS	10	72	**3l** (30:70)
13	**1j** 4-F-C_6H_4	**2b**	NaHMDS	10	94	**3m** (32:68)
14[c]	**1a** Ph	**2c** R^1 = Ph R^2 = Ph	NaHMDS	180	99	**3n**
15[c]	**1j** 4-F-C_6H_4	**2c**	NaHMDS	180	97	**3o**
16	**1a** Ph	**2d** R^1, R^2 = -$(CH_2)_6$-	NaHMDS	90	48	**3p**

[a] Isolated yields. [b] Diastereomers were separated by column chromatography. [c] Reaction performed at −78 °C to rt.

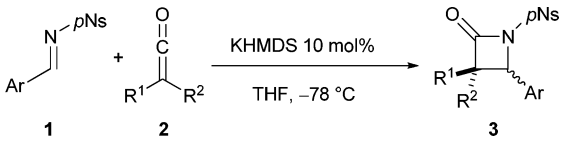


Scheme 2 Reaction of aldehydes with NaHMDS.[4g]

the results with NaHMDS and to eliminate the possibility that NaOTMS is formed with the ketene in analogy to Scheme 2. The yield and the diastereoselectivity were lower compared to the NaHMDS catalyzed reaction, but nevertheless NaOTMS showed good catalytic activity.

Commonly used tertiary amines were also applied in the reaction in order to compare their catalytic activity to MHMDS. In all cases poor yields were obtained under the reaction conditions (Table 1, entries 10–13). The reactions of tertiary amines with such highly substituted ketenes are normally performed over several hours at room temperature or on heating.[7f,7t,7u,7v] In the absence of a catalyst no reaction took place (Table 1, entry 14). An attempt to use a tosyl protected analogue of **1a** in the reaction gave an unidentified mixture of compounds and not the desired product.

Next, several imines and ketenes were used in the Staudinger reaction under the optimized conditions (Table 2, Scheme 3). In general all imines gave the corresponding products in significant yields and diastereoselectivity with the *cis*-adduct prevailing. Exceptions were the imines **1c**, **1e** and **1h** which gave good yields,

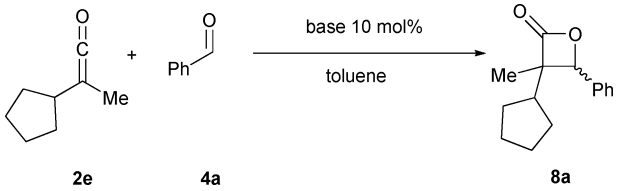


Scheme 3 Staudinger reaction with different imines and ketenes.

but a lower diastereoselectivity. In several cases the formation of the product was completed in less than 10 min.

Also, different disubstituted ketenes were applied in the reaction. Changing from an ethyl to a methyl substituent in the ketene gave the desired product in good yield and diastereoselectivity (Table 2, entry 12). The 1,1′-diphenylketene **2c** had a lower reactivity and reacted with imines **1a** and **1j** at room temperature in 98% yield (Table 2, entries 14 and 15). As an example for an alkyl-alkyl substituted ketene, imine **1a** was reacted with ketene **2d** to give the product in 49% yield (Table 2, entry 16). The lower yields of **3l** and **3p** can be attributed to the alternative possibility of oligomerization and dimerization of the ketene. In all cases the diketone dimers of the corresponding ketenes were observed.[13] The possible β-alkenyl-β-lactone dimers were not found.[14]

Due to the results for the Staudinger cycloaddition, we were interested to see whether NaHMDS has a catalytic effect in the formal [2+2] cycloaddition of ketenes and aldehydes. We focused on the ketene/aldehyde system shown in Scheme 4. Since there was no solubility issue expected, as for the Staudinger reaction, and due to the observation that in toluene a higher diastereomeric ratio was achieved (Table 1, entry 3), it was decided to carry out the subsequent cycloaddition in toluene. In analogy to other reports it was found with the presented catalytic system that aryl-aryl and aryl-alkyl ketenes were not active enough to react with benzaldehydes.[8h,8k] Therefore,



Scheme 4 Base catalyzed [2+2] reaction with ketene and benzaldehyde.

Table 3 Base catalyzed [2+2] reaction with ketene **2e** and aldehyde **4a**[a]

entry	base	t [°C]	time	yield [%][b]	*trans*:*cis*[c]
1	NaHMDS	−78	1 h	30	33:67
2	KHMDS	−78	1 h	36	22:78
3	LiHMDS	−78	1 h	0	—
4	KO*t*Bu	−78 to −20	5 h	traces	—
5	NaOTMS	−78	5 h	0	—
6	NaHMDS	−78 to rt	5 h	99	50:50
7	KHMDS	−78 to rt	5 h	99	50:50
8	KO*t*Bu	−78 to rt	5 h	54	37:63
9	NaOTMS	−10 to rt	5 h	98	50:50
10	—	−78 to rt	5 h	0	—

[a] Ketene (2 equiv.) in a 0.27 M toluene solution. [b] Isolated yield. [c] Determined by ^{1}H-NMR.

alkyl-alkyl ketenes were used in the reaction. Ketene **2e** was prepared from 2-cyclopentylpropanoylchloride in toluene with 1 equiv. of DABCO. After 3 h at 80 °C ketene **2e** was vacuum transferred together with the solvent to give a 0.27 M solution.

First, reactions with NaHMDS or KHMDS as catalysts were carried out at −78 °C for 1 h to give the product in low yields. With LiHMDS no product was obtained (Table 3, entries 1–3). In addition, KO*t*Bu was tested as a hindered non-nucleophilic base to give only traces of product at −20 °C. When the reaction was repeated with KHMDS and NaHMDS and the reaction mixture was allowed to warm to room temperature, quantitative yields were obtained. However, the diastereoselectivity decreased. With KO*t*Bu a yield of 54% was isolated at room temperature. In the absence of a catalyst no conversion occurred (Table 3, entry 10).

In order to exclude the possibility that NaOTMS is generated according to Scheme 2, a control reaction with NaOTMS as the catalyst was performed at −78 °C and no conversion was observed. If NaOTMS is applied as the catalyst between −10 °C and room temperature, product **8a** is formed in 98% yield (Table 3, entries 5 and 9). Thus, NaOTMS is less active than NaHMDS. Since NaHMDS, KHMDS and NaOTMS gave excellent yields, but a 50:50 ratio of diastereomers, when the reaction was warmed up to room temperature (Table 3, entries 6, 7 and 9) it is not possible to rule out completely that some NaOTMS was generated from NaHMDS at room temperature according to Scheme 2. However, the reaction in Scheme 2 normally proceeds at higher temperatures than room temperature and in the case of KHMDS even higher temperatures are needed.[4g]

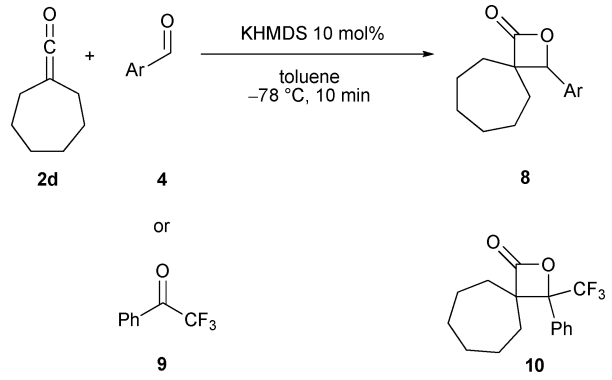
In addition, ketene **2d**[7e,15] was tested in the reaction with benzaldehyde, beginning with experiments at −78 °C or room temperature in the absence of a catalyst. No conversion into the product **8b** was observed. However, with 10 mol% KHMDS the less hindered ketene **2d** displayed with several aldehydes (Table 4) a far higher reactivity than ketene **2e**. Thus, the reactions were complete after 10 min to give the desired products (Scheme 5). Furthermore, it was even possible to apply α,α,α-trifluoroacetophenone (**9**) in the reaction with ketene **2d** and to isolate the tetrasubstituted β-lactone **10** in 49% yield (Table 4, entry 7).

Prolonged stirring did not result in a higher yield due to competing dimerization of the ketene to the corresponding diketone. Electron-rich and -deficient aldehydes gave similar yields. Furthermore, a reaction with ketene **2d**, benzaldehyde (**4a**) and

Table 4 KHMDS catalyzed Wynberg reaction with ketene **2d**[a]

entry	Ar	yield [%][b]	product
1	**4a** Ph	59	**8b**
2	**4b** 2-Me-C_6H_4	60	**8c**
3	**4c** 4-Cl-C_6H_4	60	**8d**
4	**4d** 4-Me-C_6H_4	56	**8e**
5	**4e** 4-CF_3-C_6H_4	55	**8f**
6	**4f** 4-F-C_6H_4	61	**8g**
7[c]	**9** PhCOCF3	49	**10**

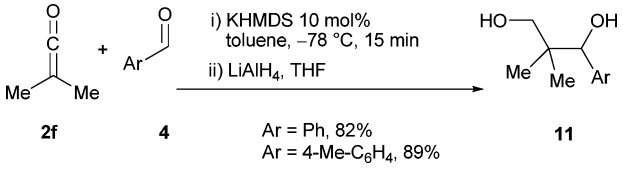
[a] Ketene **2d** (2 equiv.). [b] Isolated yield. [c] −78 °C to rt.



Scheme 5 KHMDS catalyzed Wynberg reaction with ketene **2d**.

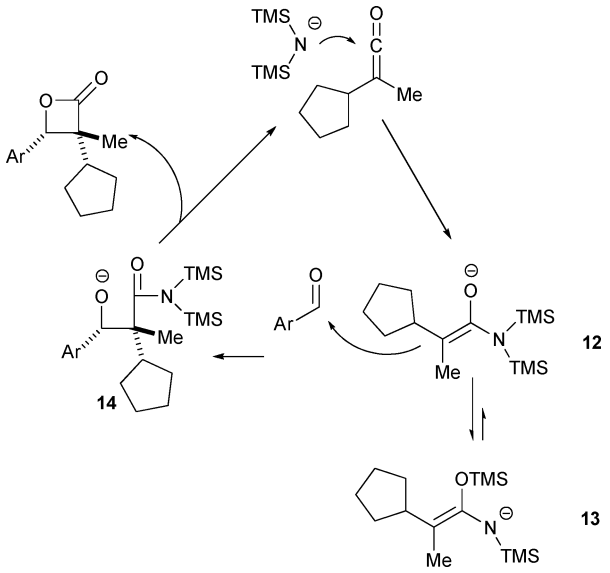
10 mol% NaOTMS at −78 °C gave the desired product in 32% yield after 10 min.

In addition, ketene **2f**[7e,15] was reacted with benzaldehyde or *para*-methylbenzaldehyde. The reactions were complete after 15 min. For easier handling, the products were directly transformed to diols **11** with $LiAlH_4$, with an overall yield of 82 and 89%, respectively (Scheme 6).



Scheme 6 KHMDS catalyzed Wynberg reaction.

Based on the present results, the mechanism in Scheme 7 can be proposed for the reaction of aldehydes with ketenes. After the initial nucleophilic attack of the HMDS anion at the ketene, the amide enolate **12** is formed, which obviously must allow a 1,3 silyl shift to anion **13**. The process would be encouraged by the oxophilicity of silicon. However, this rearrangement could be slow or lead to an equilibrating mixture from which **12** is consumed by the aldehyde. Taking into consideration that the HMDS group in enolate **12** is far larger than the cyclopentyl ring, the aldehyde approaches from the side opposite to the HMDS group and the *cis* product is formed, which is observed in the majority of examples of Lewis base catalysed [2+2] cycloadditions of ketenes with imines or aldehydes.[7,8]



Scheme 7 Proposed mechanism.

Conclusions

In conclusion it has been shown that potassium and sodium hexamethyldisilazane amides can act as highly active Lewis base catalysts in the formal [2+2] cycloaddition of ketenes with imines or aldehydes. The Staudinger cycloaddition was completed in a short time of 5 to 15 min at −78 °C. The useful *para*-nosyl group can be removed in high yield under mild conditions.[16] The speed and simplicity of the reported procedure makes it a valuable tool for preparing libraries of β-lactams and β-lactones. It was also possible to obtain a tetrasubstituted β-lactone *via* the Wynberg reaction. In addition, it was shown that KO*t*Bu and NaOTMS are also good Lewis base catalysts for these cycloadditions. These findings may encourage the exploration of tandem reactions with these bases or the development of chiral analogues.

Experimental

General experimental

All reactions were conducted under an atmosphere of dry nitrogen. Glassware was dried in an oven or flame-dried under vacuum prior to use. THF was distilled from sodium benzophenone ketyl. Toluene was distilled from sodium. Reactions were monitored by TLC with MERCK Silica gel 60 F_{254} plates. Flash column chromatography was performed on silica gel 60 (70–230 mesh ASTM) from MERCK. Ketenes **2**[7e,8h,15] and imines **1**[12] were prepared according to literature procedures. Aldehydes **4** were distilled or sublimed. All other chemicals, were purchased from commercial sources. Melting points were taken on a Dr. Tottoli apparatus from BÜCHI and are uncorrected. Infrared spectra were recorded on a Vector 22 FT-IR from BRUKER. The absorption of solids was measured by potassium bromide pellets, the absorption of liquids by using a thin layer between sodium chloride plates. ^{1}H-NMR spectra were taken on an AMX 400 (400 MHz) or an AC 250 P (200 MHz) from BRUKER in $CDCl_3$ unless otherwise stated. ^{13}C-NMR spectra were taken on an AMX 400 (100 MHz) or on an AC 250 P (50 MHz) from BRUKER in $CDCl_3$ unless otherwise stated.

General experimental procedure for the Staudinger cycloaddition. An imine **1** (0.1 mmol) and a ketene **2** (0.25 mmol) were dissolved in dry THF (1 mL) and cooled down to −78 °C. KHMDS or NaHMDS (0.01 mmol) was added, and the reaction was monitored by TLC. After total conversion the reaction mixture was sujected to column chromatography and the products were eluted with 1:8 ethyl acetate/petrol ether to give the desired diastereomers mostly as white solids (yields: 48–99%) For yields and ratios see Tables 1 and 2.

3a: *trans*-Isomer: white crystals, mp 144 °C. ^{1}H NMR (200 MHz): $\delta = 0.57$ (t, $J = 7.4$ Hz, 3 H), 1.25–1.43 (m, 1 H), 1.64–1.89 (m, 1 H), 5.24 (s, 1 H), 7.21–7.44 (m, 10 H), 8.12 (d, $J = 8.9$ Hz, 2 H), 8.34 (d, $J = 8.98$ Hz, 2 H). ^{13}C NMR (50 MHz): $\delta =$ 8.7, 27.1, 68.1, 69.9, 124.6, 126.2, 127.2, 128.1, 128.9, 129.2, 129.3, 133.6, 137.4, 143.9, 151.0, 168.6. IR (KBr) ν/cm^{-1}: 1792 (C=O). MS (ES$^+$): m/z = 459.1 [M + Na]$^+$ Anal. Calcd for $C_{23}H_{20}N_2O_5S$: C, 63.29; H, 4.62; N, 6.42%. Found: C, 63.20; H, 4.67; N, 6.35%.

cis-Isomer: white crystals, mp 144–145 °C. ^{1}H NMR (200 MHz): $\delta = 0.94$ (t, $J = 7.4$ Hz, 3 H), 2.20 (q, $J = 7.4$ Hz, 2 H), 5.15 (s, 1 H), 6.70–6.76 (m, 2 H), 6.82–6.91 (m, 2 H), 6.94–7.16 (m, 6 H), 7.95 (d, $J = 8.9$ Hz, 2 H), 8.26 (d, $J = 8.9$ Hz, 2 H). ^{13}C NMR (50 MHz): $\delta = 9.3$, 32.6, 69.1, 70.3, 124.4, 127.2, 127.4, 128.2, 128.2, 128.3, 128.9, 129.0, 133.7, 134.5, 144.4, 150.8, 167.8. IR (KBr) ν/cm^{-1}: 1792 (C=O). MS (ES$^+$): m/z = 459.1 [M + Na]$^+$. Anal. Calcd for $C_{23}H_{20}N_2O_5S$: C, 63.29; H, 4.62; N, 6.42%. Found: C, 63.38; H, 4.73; N, 6.28%.

3b: *trans*-Isomer: white crystals, mp 107 °C. ^{1}H NMR (400 MHz): $\delta = 0.83$ (t, $J = 8.0$ Hz, 3 H), 2.09–2.17 (m, 1 H), 2.24–2.33 (m, 1 H), 5.64 (s, 1 H), 6.70–6.72 (m, 1 H), 6.81–6.84 (m, 1 H), 6.95–6.98 (m, 2 H), 7.03–7.07 (m, 3 H), 7.29–7.23 (m, 2 H), 8.22 (d, $J = 8.8$ Hz, 2 H), 8.43 (d, $J = 8.8$ Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 9.3$, 30.7, 64.7, 71.5, 124.8, 126.9, 128.5, 129.3, 129.4, 129.7, 132.3, 133.1, 134.1, 143.8, 151.2, 168.4. IR (KBr) ν/cm^{-1}: 1787 (C=O). MS (ES$^+$): m/z = 493.1 [M + Na]$^+$. Anal. Calcd for ($C_{23}H_{19}ClN_2O_5S$): C, 58.66; H, 4.07; N, 5.95%. Found: C, 58.45; H, 4.05; N, 5.97%.

cis-Isomer: white crystals, mp 107 °C. ^{1}H NMR (200 MHz): $\delta = 0.59$ (t, $J = 7.4$ Hz, 3 H), 1.70 (q, $J = 7.3$ Hz, 2 H), 5.56 (s, 1 H), 7.03–7.07 (m, 5 H), 7.34–7.48 (m, 4 H), 8.15 (d, $J = 8.8$ Hz, 2 H), 8.37 (d, $J = 8.8$ Hz, 2 H). ^{13}C NMR (50 MHz): $\delta = 8.6$, 25.4, 64.7, 69.5, 124.7, 126.7, 127.9, 128.3, 130.0, 129.2, 132.2, 133.1, 133.9, 143.6, 151.1, 168.1. IR (KBr) ν/cm^{-1}: 1793 (C=O). MS (ES$^+$): m/z = 493.1 [M + Na]$^+$. Anal. Calcd for ($C_{23}H_{19}ClN_2O_5S$): C, 58.66; H, 4.07; N, 5.95%. Found: C, 58.71; H, 4.09; N, 5.81%.

3c: *trans*-Isomer: white crystals, mp 116 °C. ^{1}H NMR (200 MHz): $\delta = 0.64$ (t, $J = 7.6$ Hz, 3 H), 1.50–1.68 (m, 1 H), 1.85–2.03 (m, 1 H), 5.53 (s, 1 H), 7.04–7.11 (m, 2 H), 7.24–7.37 (m, 6 H), 8.10 (d, $J = 9.0$ Hz, 2 H), 8.34 (d, $J = 9.2$ Hz, 4 H). ^{13}C NMR (50 MHz): $\delta = 8.7$, 27.7, 65.8, 68.3, 124.5, 126.2, 126.7, 127.5, 127.9, 128.2, 129.2, 129.2, 136.5, 137.1, 144.0, 168.2. IR (KBr) ν/cm^{-1}: 1782 (C=O). MS (ES$^+$): m/z = 465.0 [M + Na]$^+$. Anal. Calcd for ($C_{21}H_{18}N_2O_5S_2$): C, 57.00; H, 4.10; N, 6.33%. Found: C, 56.99; H, 4.10; N, 6.30%.

cis-Isomer: white crystals, mp 124 °C. ^{1}H NMR (200 MHz): $\delta = 0.97$ (t, $J = 7.2$ Hz, 3 H), 2.25 (q, $J = 8.0$ Hz, 2 H), 5.49 (s, 1 H), 6.73–6.75 (m, 2 H), 6.97–7.04 (m, 3 H), 7.11–7.18 (m, 3 H), 7.93 (d, $J = 9.04$ Hz, 2 H), 8.25 (d, $J = 9.04$ Hz, 2 H). ^{13}C NMR (50 MHz): $\delta = 9.3$, 32.4, 64.9, 70.5, 124.4, 126.4, 127.2, 127.9, 128.5, 128.9, 129.1, 134.5, 137.2, 144.4, 150.8, 167.2. IR (KBr)

ν/cm^{-1}: 1790 (C=O). MS (ES$^+$): m/z = 465.0 [M + Na]$^+$. Anal. Calcd for ($C_{21}H_{18}N_2O_5S_2$): C, 57.00; H, 4.10; N, 6.33%. Found: C, 57.13; H, 4.15; N, 6.26%.

3d: *trans*-Isomer: white crystals, mp 182 °C. ^{1}H NMR (200 MHz): δ = 0.66 (t, J = 7.4 Hz, 3 H), 1.26–1.43 (m, 1 H), 1.58–1.78 (m, 1 H), 5.82 (s, 1 H), 7.05–7.10 (m, 2 H), 7.34–7.38 (m, 3 H), 7.43–7.63 (m, 5 H), 7.87–7.97 (m, 2 H), 8.27 (d, J = 9.0 Hz, 2 H), 8.46 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 8.9, 24.1, 68.5, 68.8, 122.9, 124.8, 125.1, 125.2, 126.5, 126.9, 128.6, 129.5, 129.5, 129.6, 129.7, 130.9, 133.9, 136.6, 144.0, 169.7. IR (KBr) ν/cm^{-1}: 1787 (C=O). MS (ES$^+$): m/z = 509.2 [M + Na]$^+$. Anal. Calcd for ($C_{27}H_{22}N_2O_5S$): C, 66.65; H, 4.56; N, 5.76%. Found: C, 66.77; H, 4.78; N, 5.59%.

cis-Isomer: white crystals, mp 186 °C. ^{1}H NMR (200 MHz): δ = 0.97 (t, J = 7.6 Hz, 3 H), 2.26–2.47 (m, 2 H), 6.05 (s, 1 H), 6.69–6.99 (m, 6 H), 7.50–7.69 (m, 4 H), 7.83 (d, J = 7.8 Hz, 1 H), 8.02 (d, J = 8.2 Hz, 1 H), 8.15 (d, J = 9.0 Hz, 2 H), 8.38 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 9.5, 31.2, 64.9, 71.6, 121.7, 124.7, 125.1, 126.1, 126.8, 127.2, 127.6, 128.1, 129.0, 129.3, 129.5, 129.6, 131.3, 133.5, 134.1, 138.3, 144.4, 168.6. IR (KBr) ν/cm^{-1}: 1782 (C=O). MS (ES$^+$): m/z = 509.2 [M + Na]$^+$. Anal. Calcd for ($C_{27}H_{22}N_2O_5S$): C, 66.65; H, 4.56; N, 5.76%. Found: C, 66.58; H, 4.87; N, 5.54%.

3e: *trans*-Isomer: white crystals, mp = 155 °C. ^{1}H NMR (400 MHz): δ = 0.56 (t, J = 7.2 Hz, 3 H), 1.31–1.40 (m, 1 H), 1.74–1.83 (m, 1 H), 5.42 (s, 1 H), 7.30–7.41 (m, 6 H), 7.54–7.58 (m, 2 H), 7.73–7.77 (m, 2 H), 7.87–7.91 (m, 2 H), 8.13 (d, J = 8.8 Hz, 2 H), 8.34 (d, J = 8.8 Hz, 2 H). ^{13}C NMR (100 MHz): δ = 8.6, 27.0, 29.7, 68.2, 69.9, 124.2, 124.4, 126.2, 126.7, 126.9, 127.0, 127.8, 127.9, 128.0, 128.7, 129.0, 129.1, 130.8, 132.9, 133.4, 137.3, 143.9, 150.9, 168.4. IR (KBr) ν/cm^{-1}: 1783 (C=O). MS (ES$^+$): m/z = 508.8 [M + Na]$^{+\cdot}$. Anal. Calcd for $C_{27}H_{22}N_2O_5S$: C 66.65; H 4.56; N 5.76%. Found: C 66.70; H 4.43; N 5.71%.

cis-Isomer: white crystals, mp = 177 °C. ^{1}H NMR (200 MHz): δ = 0.99 (t, J = 7.4 Hz, 3 H), 2.17–2.36 (m, 2 H), 5.33 (s, 1 H), 6.51 (d, J = 8.6 Hz, 1 H), 6.89–7.01 (m, 5 H), 7.29 (d, J = 8.6 Hz, 1 H), 7.41–7.50 (m, 3 H), 7.57–7.69 (m, 2 H), 7.86 (d, J = 9.2 Hz, 2 H), 8.12 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 9.2, 32.8, 69.3, 70.0, 124.2, 124.5, 126.6, 126.9, 127.1, 127.3, 127.7, 127.7, 128.2, 128.6, 128.8, 130.9, 132.5, 133.0, 134.3, 144.2, 150.6, 167.6. IR (KBr) ν/cm^{-1}: 1788 (C=O). MS (ES$^+$): m/z = 995.0 [2M + Na]$^+$. Anal. Calcd for $C_{27}H_{22}N_2O_5S$: C 66.65; H 4.56; N 5.76%. Found: C 66.78; H 4.55; N 5.80%.

3f: *trans*-Isomer: white crystals, mp 142 °C. ^{1}H NMR (200 MHz): δ = 0.57 (t, J = 7.4 Hz, 3 H), 1.25–1.43 (m, 1 H), 1.59–1.83 (m, 1 H), 2.39 (s, 3 H), 5.21 (s, 1 H), 7.21–7.43 (m, 9 H), 8.12 (d, J = 9.0 Hz, 2 H), 8.35 (d, J = 9.04 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 8.7, 21.4, 27.2, 68.0, 70.0, 124.6, 126.2, 127.2, 128.1, 129.2, 130.5, 137.5, 139.2, 144.0, 151.1, 168.7. IR (KBr) ν/cm^{-1}: 1785 (C=O). MS (ES$^+$): m/z = 473 [M + Na]$^+$. Anal. Calcd for ($C_{24}H_{22}N_2O_5S$): C, 63.98; H, 4.92; N, 6.22%. Found: C, 64.05; H, 5.17; N, 6.02%.

c*is*-Isomer: white crystals, mp 147 °C. ^{1}H NMR (200 MHz): δ = 0.93 (t, J = 8.0 Hz, 3 H), 2.18 (q, J = 7.2 Hz, 2 H), 2.20 (s, 3 H), 5.11 (s, 1 H), 6.60 (d, J = 8.0 Hz, 2 H), 6.78 (d, J = 8.0 Hz, 2 H), 6.85–6.89 (m, 2 H), 7.02–7.09 (m, 3 H), 7.87 (d, J = 9.0 Hz, 2 H), 8.18 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 9.3, 21.2, 32.8, 69.2, 70.0, 124.3, 127.3, 127.4, 128.2, 128.3, 128.9, 129.0, 130.5, 134.6, 138.9, 144.4, 150.8, 167.9. IR (KBr) ν/cm^{-1}: 1781 (C=O). MS (ES$^+$): m/z = 473 [M + Na]$^+$. Anal. Calcd for ($C_{24}H_{22}N_2O_5S$): C, 63.98; H, 4.92; N, 6.22%. Found: C, 63.99; H, 5.02; N, 6.21%.

3g: *trans*-Isomer: white crystals, mp = 163 °C. ^{1}H NMR (200 MHz): δ = 0.59 (t, J = 7.4 Hz, 3 H), 1.25–1.43 (m, 1 H), 1.62–1.80 (m, 1 H), 5.17 (s, 1 H), 7.16–7.21 (m, 2 H), 7.29–7.35 (m, 5 H), 7.42 (d, J = 8.6 Hz, 2 H), 8.14 (d, J = 9.0 Hz, 2 H), 8.36 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 8.6, 27.1, 68.0, 69.1, 124.5, 126.0, 128.1, 128.4, 129.0, 129.1, 129.2, 132.2, 135.1, 136.9, 143.5, 151.0, 168.2. IR (KBr) ν/cm^{-1}: 1789 (C=O). MS (ES$^+$): m/z = 493.0 [M + Na]$^+$. Anal. Calcd for $C_{23}H_{19}ClN_2O_5S$: C 58.66; H 4.07; N 5.93%. Found: C 58.79; H 3.95; N 5.92%.

cis-Isomer: white crystals, mp = 134 °C. ^{1}H NMR (200 MHz): δ = 0.90 (t, J = 7.4 Hz, 3 H), 2.16 (q, J = 7.4 Hz, 2 H), 5.11 (s, 1 H), 6.72 (d, J = 8.4 Hz, 2 H), 6.83–6.87 (m, 2 H), 7.01 (d, J = 8.6 Hz, 2 H), 7.05–7.12 (m, 2 H), 8.02 (d, J = 9.2 Hz, 2 H), 8.33 (d, J = 9.2 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 9.1, 32.2, 68.2, 70.3, 124.4, 127.0, 127.6, 128.4, 128.9, 129.2, 132.4, 133.9, 134.8, 144.1, 150.9, 167.5. IR (KBr) ν/cm^{-1}: 1792 (C=O). MS (ES$^+$): m/z = 493.1 [M + Na]$^+$. Anal. Calcd for $C_{23}H_{19}ClN_2O_5S$: C 58.66; H 4.07; N 5.93%. Found: C 58.80; H 4.09; N 6.05%.

3h: *trans*-Isomer: white crystals, mp = 158–159 °C. ^{1}H NMR (200 MHz): δ = 0.61 (t, J = 7.2 Hz, 3 H), 1.23–1.42 (m, 1 H), 1.60–1.78 (m, 1 H), 5.22 (s, 1 H), 7.16–7.20 (m, 2 H), 7.31–7.37 (m, 3 H), 7.53 (d, J = 8.0 Hz, 2 H), 7.72 (d, J = 8.2 Hz, 2 H), 8.16 (d, J = 9.0 Hz, 2 H), 8.38 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 8.6, 27.0, 68.2, 69.1, 124.6, 125.9, 126.0, 127.4, 128.3, 129.0, 129.2, 136.7, 137.8, 143.3, 151.0, 168.0. IR (KBr) ν/cm^{-1}: 1783 (C=O). MS (ES$^+$): m/z = 527.0 [M + Na]$^+$. Anal. Calcd for $C_{24}H_{19}F_3N_2O_5S$: C 57.14; H 3.80; N 5.55%. Found: C 56.98; H 3.85; N 5.40%.

cis-Isomer: white crystals, mp = 131 °C. ^{1}H NMR (200 MHz): δ = 0.91 (t, J = 7.4 Hz, 3 H), 2.17 (q, J = 7.0 Hz, 2 H), 5.16 (s, 1 H), 6.81–6.81 (m, 2 H), 6.94 (d, J = 8.0 Hz, 2 H), 7.10–7.30 (m, 3 H), 7.30 (d, J = 8.0 Hz, 2 H), 8.37 (d, J = 9.0 Hz, 2 H), 8.35 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 9.1, 31.9, 68.0, 70.7, 124.5, 125.0, 125.1, 125.2, 127.0, 127.7, 128.1, 128.4, 128.9, 133.6, 138.0, 143.9, 150.9, 167.4. IR (KBr) ν/cm^{-1}: 1796 (C=O). MS (ES$^+$): m/z = 526.8 [M + Na]$^+$. Anal. Calcd for $C_{24}H_{19}F_3N_2O_5S$: C 57.14; H 3.80; N 5.55%. Found: C 56.87; H 3.85; N 5.39%.

3i: *trans*-Isomer: white crystals, mp = 168 °C. ^{1}H NMR (200 MHz): δ = 0.61 (t, J = 7.4 Hz, 3 H), 1.22–1.42 (m, 1 H), 1.56–1.76 (m, 1 H), 5.18 (s, 1 H), 7.12–7.17 (m, 2 H), 7.31–7.37 (m, 3 H), 7.55 (d, J = 8.2 Hz, 2 H), 7.78 (d, J = 8.4 Hz, 2 H), 8.16 (d, J = 9.0 Hz, 2 H), 8.38 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 8.6, 27.0, 68.4, 69.0, 113.2, 118.0, 124.6, 125.8, 127.7, 128.4, 129.0, 129.3, 132.6, 136.4, 139.1, 143.1, 151.1, 167.8. IR (KBr) ν/cm^{-1}: 1797 (C=O). MS (ES$^+$): m/z = 484.09 [M + Na]$^+$. Anal. Calcd for $C_{24}H_{19}N_3O_5S$: C 62.46; H 4.15; N 9.11%. Found: C 62.61; H 4.19; N 9.15%.

cis-Isomer: white crystals, mp = 103–104 °C. ^{1}H NMR (200 MHz): δ = 0.87 (t, J = 7.4 Hz, 3 H), 2.05–2.25 (m, 2 H), 5.13 (s, 1 H), 6.80–6.86 (m, 2 H), 6.99 (d, J = 8.4 Hz, 2 H), 7.04–7.09 (m, 3 H), 7.37 (d, J = 8.4 Hz, 2 H), 8.13 (d, J = 9.0 Hz, 2 H), 8.41 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 9.1, 31.5, 67.8, 71.1, 112.3, 112.6, 118.0, 124.7, 126.9, 127.9, 128.2, 128.6, 129.0, 131.9, 133.3, 139.5, 143.7, 151.1, 167.2. IR (KBr) ν/cm^{-1}: 1786 (C=O). MS (ES$^+$): m/z = 484.09 [M + Na]$^+$. Anal. Calcd for $C_{24}H_{19}N_3O_5S$: C 62.46; H 4.15; N 9.11%. Found: C 62.45; H 4.19; N 9.36%.

3j: *trans*-Isomer: white crystals, mp = 79 °C. ^{1}H NMR (200 MHz): δ = 0.59 (t, J = 7.4 Hz, 3 H), 1.25–1.43 (m, 1 H), 1.63–1.81 (m, 1 H), 5.19 (s, 1 H), 7.09–7.21 (m, 4 H), 7.29–7.39 (m, 5 H), 8.13 (d, J = 9.2 Hz, 2 H), 8.36 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 8.5, 27.0, 68.0, 69.1, 115.7, 116.2, 124.5, 126.0, 128.1, 128.7, 128.9, 129.0, 129.1, 129.3, 129.4, 137.0, 143.6, 168.3. IR (KBr) ν/cm^{-1}: 1786 (C=O). MS (ES$^+$): m/z = 477.0 [M + Na]$^+$.

cis-Isomer: white crystals, mp = 124 °C. ^{1}H NMR (200 MHz): δ = 0.91 (t, J = 7.4 Hz, 3 H), 2.16 (q, J = 7.4 Hz, 2 H), 5.13 (s, 1 H), 6.72–6.76 (m, 4 H), 6.82–6.87 (m, 2 H), 7.04–7.11 (m, 3 H), 8.01 (d, J = 9.0 Hz, 2 H), 8.33 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 9.2, 32.2, 68.2, 70.3, 115.0, 115.4, 124.4, 127.1, 127.5, 128.3, 128.9, 129.6, 129.6, 129.7, 134.1, 144.2, 150.8, 160.2, 165.1, 167.6. IR (KBr) ν/cm^{-1}: 1784 (C=O). MS (ES$^+$): m/z = 477.0 [M + Na]$^+$.

3k: *trans*-Isomer: light yellow crystals, mp 143 °C. ^{1}H NMR (200 MHz): δ = 0.59 (t, J = 7.4 Hz, 3 H), 1.26–1.49 (m, 1 H), 1.69–1.87 (m, 1 H), 3.86 (s, 3 H), 3.92 (s, 3 H), 5.16 (s, 1 H), 6.84 (s, 1 H), 6.88–6.89 (m, 2 H), 7.18–7.39 (m, 5 H), 8.13 (d, J = 9.0 Hz, 2 H), 8.35 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 8.7, 27.1, 56.1, 56.2, 68.2, 69.9, 110.2, 111.3, 119.9, 124.6, 125.9, 126.2, 128.1, 129.2, 137.5, 143.9, 149.3, 149.8, 151.1, 168.8. IR (KBr) ν/cm^{-1}: 1793 (C=O). MS (ES$^+$): m/z = 518.8 [M + Na]$^+$, 829.0. Anal. Calcd for ($C_{25}H_{24}N_2O_7S$): C, 60.47; H, 4.87; N, 5.64%. Found: C, 60.41; H, 4.83; N, 5.63%.

cis-Isomer: yellow crystals, mp 146 °C. ^{1}H NMR (200 MHz): δ = 0.94 (t, J = 7.4 Hz, 3 H), 2.18 (q, J = 7.4 Hz, 2 H), 3.21 (s, 3 H), 3.79 (s, 3 H), 5.08 (s, 1 H), 5.82 (s, 1 H), 6.57–6.59 (m, 2 H), 6.84–6.92 (m, 2 H), 7.06–7.09 (m, 3 H), 7.93 (d, J = 9.0 Hz, 2 H), 8.26 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 9.3, 32.6, 55.4, 55.9, 69.2, 69.9, 110.3, 110.6, 121.8, 124.3, 125.7, 127.2, 127.5, 128.4, 129.0, 129.2, 134.9, 144.4, 148.5, 149.5, 150.8, 167.9. IR (KBr) ν/cm^{-1}: 1787 (C=O). MS (ES$^+$): m/z = 518.8 [M + Na]$^+$, 829.0. Anal. Calcd for ($C_{25}H_{24}N_2O_7S$): C, 60.47; H, 4.87; N, 5.64%. Found: C, 60.47; H, 4.90; N, 5.67%.

3l: *trans*-Isomer: white crystals, mp 163 °C. ^{1}H NMR (200 MHz): δ = 1.18 (s, 3 H), 5.28 (s, 1 H), 7.20–7.42 (m, 10 H), 8.15 (d, J = 9.0 Hz, 2 H), 8.37 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 20.0, 64.1, 70.0, 124.6, 125.4, 127.0, 128.2, 129.0, 129.2, 129.3, 129.4, 133.6, 139.6, 144.0, 151.1, 169.1. IR (KBr) ν/cm^{-1}: 1787 (C=O). MS (ES$^+$): m/z = 445.1 [M + Na]$^+$. Anal. Calcd for ($C_{22}H_{18}N_2O_5S$): C, 62.55; H, 4.29; N, 6.63%. Found: C, 63.19; H, 4.64; N, 6.63%.

cis-Isomer: white crystals, mp 142 °C. ^{1}H NMR (200 MHz): δ = 1.81 (s, 3 H), 5.12 (s, 1 H), 6.71–6.77 (m, 2 H), 6.86–6.93 (m, 2 H), 6.95–7.16 (m, 6 H), 7.98 (d, J = 9.0 Hz, 2 H), 8.29 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 25.4, 66.0, 71.1, 124.5, 126.8, 127.6, 127.9, 128.3, 128.5, 129.0, 129.1, 133.6, 135.8, 144.2, 150.9, 168.5. IR (KBr) ν/cm^{-1}: 1791 (C=O). MS (ES$^+$): m/z = 445.1 [M + Na]$^+$. Anal. Calcd for ($C_{22}H_{18}N_2O_5S$): C, 62.55; H, 4.29; N, 6.63%. Found: C, 63.14; H, 4.60; N, 6.50%.

3m: *trans*-Isomer: white crystals, mp = 59 °C. ^{1}H NMR (400 MHz): δ = 1.18 (s, 3 H), 5.23 (s, 1 H), 7.11–7.19 (m, 4 H), 7.28–7.35 (m, 5 H), 8.16 (d, J = 8.8 Hz, 2 H), 8.38 (d, J = 8.8 Hz, 2 H). ^{13}C NMR (100 MHz): δ = 19.8, 29.7, 64.0, 69.3, 115.9, 116.2, 124.6, 125.2, 128.2, 128.6, 128.7, 129.0, 129.3, 139.1, 143.6, 151.0, 168.8. IR (KBr) ν/cm^{-1}: 1795 (C=O).). MS (ES$^+$): m/z = 463.08 [M + Na]$^+$. HRMS Calcd for $C_{22}H_{17}FN_2O_5SNa$: 463.0740. Found: 463.0758.

cis-Isomer: white crystals, mp = 139 °C. ^{1}H-NMR (200 MHz): δ = 1.77 (s, 3 H), 5.09 (s, 1 H), 6.68–6.79 (m, 4 H), 6.85–6.91 (m, 2 H), 7.04–7.11 (m, 3 H), 8.04 (d, J = 9.0 Hz, 2 H), 8.35 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 24.9, 69.9, 70.2, 115.0, 115.5, 124.5, 126.6, 127.6, 128.5, 128.9, 129.3, 129.5, 129.6, 129.6, 135.4, 143.8, 150.9, 160.2, 165.1, 168.2. IR (KBr) ν/cm^{-1}: 1794 (C=O). MS (ES$^+$): m/z = 463.1 [M + Na]$^+$. HRMS Calcd for $C_{22}H_{17}FN_2O_5SNa$: 463.0740. Found: 463.0741.

3n: white crystals, mp 156 °C. ^{1}H NMR (200 MHz): δ = 5.86 (s, 1 H), 6.87–7.21 (m, 10 H), 7.28–7.48 (m, 5 H), 8.00 (d, J = 9.0 Hz, 2 H), 8.26 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 69.6, 73.3, 124.4, 126.9, 127.6, 127.8, 128.0, 128.3, 128.4, 129.0, 129.1, 129.2, 133.4, 135.6, 138.7, 143.9, 150.9, 166.7. IR (KBr) ν/cm^{-1}: 1781 (C=O). MS (ES$^+$): m/z = 507.0 [M + Na]$^+$. Anal. Calcd for ($C_{27}H_{20}N_2O_5S$): C, 66.93; H, 4.16; N, 5.78%. Found: C, 66.97; H, 4.31; N, 5.77%.

3o: white crystals, mp 121 °C. ^{1}H NMR (200 MHz): δ = 5.84 (s, 1 H), 6.75–6.96 (t, 6 H), 7.01–7.09. (m, 3 H), 7.28–7.44 (m, 5 H), 8.04 (d, J = 9.0 Hz, 2 H), 8.30 (d, J = 9.0 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 29.7, 68.8, 115.2, 115.6, 124.4, 126.8, 127.7, 128.3, 128.4, 128.9, 129.1, 129.5, 129.7, 135.2, 138.3, 143.6, 166.5. IR (KBr) ν/cm^{-1}: 1791 (C=O). MS (ES$^+$): m/z = 524.8 [M + Na]$^+$. Anal. Calcd for $C_{27}H_{19}FN_2O_5S$: C 64.53; H 3.81; N 5.57%. Found: C 64.83; H 3.89; N 5.67%.

3p: white crystals, mp 168 °C. ^{1}H NMR (200 MHz): δ = 1.06–1.38 (m, 4 H), 1.46–1.66 (m, 6 H), 1.72–2.02 (m, 2 H), 4.85 (s, 1 H), 7.11–7.33 (m, 5 H), 8.12 (d, J = 8.8 Hz, 2 H), 8.38 (d, J = 8.8 Hz, 2 H). ^{13}C NMR (50 MHz): δ = 22.8, 23.7, 29.0, 29.1, 30.0, 35.4, 64.3, 70.5, 124.6, 127.1, 128.8, 129.0, 129.2, 134.1, 144.2, 151.0, 171.3. IR (KBr) ν/cm^{-1}: 1787 (C=O). MS (ES$^+$): m/z = 437.2 [M + Na]$^+$. Anal. Calcd for ($C_{21}H_{22}N_2O_5S$): C, 60.85; H, 5.35; N, 6.76%. Found: C, 60.71; H, 5.47; N, 6.69%.

Preparation of cyclopentyl methyl ketene 2e. The ketene was prepared by dehydrochlorination of 2-cyclopentylpropanoyl chloride (2.73 g, 17 mmol) with DABCO (1.9 g 17 mmol) in toluene (20 mL) under a nitrogen atmosphere at 80 °C. After 3 h the reaction mixture was allowed to cool down to room temperature and the ketene and toluene were vacuum transferred into another flask. To quantify the amount of ketene generated by this procedure, 0.5 mL of yellow ketene solution was quenched with an excess of *n*-propylamine. Evaporation of the solvent and excess amine furnished 2-cyclopentyl-*N*-propylpropanamide as a white solid (24.4 mg). The concentration of ketene solution was 0.27 M. ^{1}H NMR (200 MHz) δ = 0.88 (t, J = 7.5 Hz, 3 H), 1.00–1.16 (m, 5 H), 1.43–1.61 (m, 6 H), 1.65–1.82 (m, 2 H), 1.84–1.96 (m, 2 H), 3.07–3.27 (m, 2 H), 5.83 (s, 1 H).

General experimental procedure for Table 3. To a ketene solution of **2e** (0.75 mmol, 2.82 mL toluene) was added benzaldehyde (**4a**) (30μL, 0.3 mmol) at −78 °C followed by the addition of MHMDS (0.5 M solution in toluene), NaOTMS or KO*t*Bu (0.03 mmol). After the given times and temperatures in Table 3, the reaction mixture was subjected directly to column chromatography on silica gel and the diastereomers were eluted with a 1:19 diethyl ether–petrol ether mixture to give the desired compounds as oils. For yields and diastereomeric ratios see Table 3.

8a: *trans*-Diastereomer: ^{1}H NMR (200 MHz) δ = 0.91 (s, 3 H), 1.26–1.58 (m, 2 H), 1.62–1.78 (m, 4 H), 1.79–2.06 (m, 2 H), 2.21–2.38 (m, 1 H), 5.39 (s, 1 H), 7.22–7.46 (m, 5 H); ^{13}C NMR (50 MHz) δ = 15.5, 25.5, 25.6, 27.8, 28.3, 44.3, 63.3, 79.5, 125.4, 128.3, 128.6, 135.6, 174.5. The spectral data were consistent with literature values.[8h]

cis-Diastereomer: ^{1}H NMR (200 MHz) δ = 0.89–1.29 (m, 3 H), 1.30–1.53 (m, 5 H), 1.55 (s, 3 H), 1.97–2.08 (m, 1 H), 5.30 (s, 1 H), 7.28–7.44 (m, 5 H); ^{13}C NMR (50 MHz) δ = 17.0, 25.6, 25.8, 26.7, 28.2, 39.8, 63.3, 83.7, 126.1, 128.5, 128.6, 135.6, 174.7. The spectral data were consistent with literature values.[8h]

General experimental procedure for Table 4. Ketene **2d** (93 mg, 0.75 mmol) and an aldehyde **4** or **9** (0.3 mmol) were placed into a dry Schlenk flask with dry toluene (2 mL) at −78 °C. KHMDS (0.5 M solution in toluene, 0.03 mmol, 10 mol%) was slowly added. The reaction mixture was stirred for 10 min. The solvent was removed under reduced pressure giving the crude products **8**, which were purified by column chromatography (2/98 diethyl ether/hexane) to give the desired lactones. For yields see Table 4.

8b: oil; ^{1}H NMR (400 MHz) δ = 1.25–1.42 (m, 4 H), 1.55–1.64 (m, 4 H), 1.85–1.90 (m, 2 H), 2.14–2.25 (m, 2 H), 5.30 (s, 1 H), 7.25–7.46 (m, 5 H); ^{13}C-NMR (100 MHz) δ = 22.9, 23.8, 29.1, 29.2, 30.4, 35.4, 64.0, 84.2, 125.9, 128.7, 135.5, 175.5. Spectral data were consistent with literature values.[8h]

8c: oil, ^{1}H NMR (400 MHz) δ = 1.44–1.57 (m, 9 H), 1.74–1.76 (m, 1 H), 1.90–1.94 (m, 1 H), 2.16–2.22 (m, 1 H), 2.30 (s, 3 H), 2.42–2.48 (m, 1 H), 5.40 (s, 1 H), 7.19 (d, J = 8.0 Hz) 7.27–7.35 (m, 2 H), 7.47–7.49 (m, 1 H); ^{13}C NMR (100 MHz) δ = 18.4, 22.0, 22.7, 28.4, 28.7, 30.9, 34.9, 62.7, 81.7, 124.4, 125.3, 127.1, 129.2, 128.9, 132.9, 133.1, 174.2. IR (NaCl) ν/cm^{-1} 1827, 1458, 1460, 1102, 937.

8d: oil, ^{1}H NMR (400 MHz) δ = 1.26–1.37 (m, 5 H), 1.60–1.69 (m, 4 H), 1.85–1.90 (m, 1 H), 2.13–2.19 (m, 1 H), 2.27–2.31 (m, 1 H), 5.31 (s, 1 H), 7.30 (d, J = 8.0 Hz, 2 H),7.45 (d, J = 8.0 Hz, 2 H); ^{13}C NMR (100 MHz) δ = 22.7, 23.7, 28.98, 29.03, 30.3, 35.2, 64.1, 83.4, 127.2, 128.9, 134.0, 134.4, 175.0. IR (NaCl) ν/cm^{-1} 1827, 1460, 1092, 940.

8e: oil, ^{1}H NMR (200 MHz) δ = 1.22–1.25 (m, 5 H), 1.50–1.57- (m, 4 H), 1.70–1.90 (m, 1 H), 1.90–1.94 (m, 1 H), 2.05–2.25 (m, 2 H), 2.30 (s, 3 H), 5.20 (s, 1 H), 7.05–7.18 (m, 4 H); ^{13}C NMR (50 MHz) δ = 21.4, 22.9, 23.8, 29.2, 29.8, 30.3, 35.4, 63.8, 84.3, 125.9, 129.4, 132.5, 138.5, 175.7. IR (NaCl) ν/cm^{-1} 1823, 1459, 1260, 1106, 938.

8f: oil, ^{1}H NMR (200 MHz) δ = 1.20–1.63 (m, 9 H), 1.84–1.97 (m, 1 H), 2.09–2.37 (m, 2 H), 5.34 (s, 1 H), 7.44 (d, J = 8.0 Hz, 2 H), 7.71 (d, J = 8.0 Hz, 2 H); ^{13}C NMR (50 MHz), δ = 22.7, 23.6, 28.9, 29.0, 30.4, 35.3, 64.5, 83.2, 121.2, 125.6, 125.8, 126.1, 130.4, 131.1, 139.5, 174.6. IR (NaCl) ν/cm^{-1} 1827, 1512, 1264, 1108, 939.

8g: oil, ^{1}H NMR (200 MHz) δ = 1.25–1.45 (m, 4 H), 1.63–1.68 (m, 4 H), 1.82–1.92 (m, 2 H), 2.06–2.32 (m, 2 H), 2.30 (s, 3 H), 5.28 (s, 1 H), 7.07–7.15 (m, 2 H), 7.24–7.31 (m, 2 H); ^{13}C NMR (50 MHz), δ = 22.3, 23.2, 27.8, 28.5, 29.6, 34.8, 63.5, 83.0, 115.2 (d, J = 22 Hz), 127.1 (d, J = 8 Hz), 131.1, 162.2 (d, J = 245 Hz), 174.6. IR (NaCl) ν/cm^{-1} 1826, 1512, 1459, 1261, 1109, 939.

10: oil, ^{1}H NMR (200 MHz) δ = 1.20–1.91 (m, 10 H), 2.15–2.40 (m, 2 H), 7.24–7.55 (m, 5 H); ^{13}C NMR (50 MHz), δ = 22.7, 23.1, 29.3 (q, J = 2.8 Hz), 29.5, 29.7, 34.3, 66.7, 84.7 (q, J = 30.2 Hz), 124.1 (q, J = 281.6 Hz), 125.3 (q, J = 2.2 Hz), 126.5, 128.2, 129.2, 129.4, 131.2, 172.2. IR (NaCl) ν/cm^{-1} 3055, 2987, 1845, 1422, 1266, 1179, 748.

General experimental procedure for the reaction with ketene 2f. Ketene **2f** (0.6 mmol, 1.62 mL, 0.37 M solution in THF) and aldehyde **4a** or **4d** (0.3 mmol) were added at −78 °C to toluene (2 mL) followed by the addition of KHMDS (0.03 mmol, 0.5 M solution in toluene). The reaction was monitored by TLC. After 15 min the reaction was completed. The reaction was worked up with sat. $NH_4Cl_{(aq)}$ (5 mL) and the aqueous phase was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic phases were dried (Na_2CO_3) and the solvent removed. The resulting product was dissolved in THF (5 mL) and $LiAlH_4$ (1.2 mmol) was added. After 1 h stirring the reaction was carefully quenched with 1 M NaOH (5 mL) and H_2O (5 mL). The aqueous solution was extracted with EtOAc (3 × 5 mL) and the combined phases were dried (Na_2SO_4) and the solvent removed. The crude product was purified on silica gel and the products were eluted with 1:2 diethyl ether–petrol ether mixture to give the desired compounds as white solids. The spectral data were consistent with literature values.[8h]

11a: Ar = Ph, solid, yield 82%. ^{1}H NMR (200 MHz) δ = 0.89–1.29 (m, 3 H), 1.30–1.53 (m, 5 H), 1.55 (s, 3 H), 1.97–2.08 (m, 1 H), 5.30 (s, 1 H), 7.28–7.44 (m, 5 H); ^{13}C NMR (50 MHz) δ = 17.0, 25.6, 25.8, 26.7, 28.2, 39.8, 63.3, 83.7, 127.4, 128.4, 137.1, 138.4.

11b: Ar = 4-Me-C_6H_4-, solid, yield 89%. ^{1}H NMR (200 MHz) δ = 0.81 (s, 3 H), 0.86 (s, 3 H), 2.34 (s, 3 H), 3.15 (s, 2 H), 3.48 (d, J = 10.2 Hz, 1 H), 3.58 (d, J = 10.5 Hz, 1 H), 4.59 (s, 1 H), 7.11–7.59 (m, 4 H). ^{13}C NMR (50 MHz) δ = 18.9, 21.7, 22.7, 39.0, 72.0, 82.1, 127.4, 127.5, 128.4, 137.1, 138.4.

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An imidazolinium salt as ionic liquid for medium and strong bases

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An imidazolinium salt incorporating a phenyl ring at the C-2 position has been found to be an ionic liquid suitable as a solvent for reactions involving medium and strong bases like quinuclidine and Grignard reagents.

Introduction

Ionic liquids, having by definition a melting point below 100 °C, and especially room temperature ionic liquids (RTIL) have attracted much interest in recent years as novel solvents for reactions and electrochemical processes.[1] They are considered to be "green solvents".[2] The scope of ionic liquids based on various combinations of cations and anions has dramatically increased and new salts[3–5] and solvent mixtures[6] are continually being discovered. The most commonly used liquids are based on imidazolium cations like [BMIM] (1-butyl-3-methylimidazolium) with an appropriate counter anion.

However, it has been observed that imidazolium salts, incorporating a hydrogen substituent at the C-2 position, are, in some applications where bases are involved, deprotonated. The corresponding carbenes are formed, which can cause undesired side reactions,[7] such as in the case of the Baylis–Hillman reaction.[8] Nevertheless, there are also cases where this behavior has a positive effect. In reactions where metals are used as catalysts the carbenes formed are acting as ligands and stabilizing the metal catalyst, *e.g.*, in the Suzuki reaction.[9,10] The undesired deprotonation has been partly overcome by the application of imidazolium salts with a methyl group at the C-2 position, *e.g.*, [BDMIM][PF_6] (1-butyl-2,3-dimethylimidazolium) in a Baylis–Hillman reaction.[11] Recently, it has been shown that also the C-2 methyl group of these cations can be deprotonated under mild conditions,[12] which would make these cations unsuitable for reactions involving strong bases. Therefore, Clyburne and co-workers showed for the first time that an ionic liquid, based on a phosphonium salt, can be used in reactions involving highly basic organometallic reagents giving good GC yields.[13]

Here we would like to present a second possible alternative salt for reactions involving strong bases. The novel salt can be easily prepared on a large scale from commercially available sources. During our investigation of imidazolinium salts[14] we found that some of these salts qualify as novel ionic liquids. To the best of our knowledge imidazolinium based ionic liquids with a phenyl substituent at the C-2 carbon have not been used as solvents in reactions so far. Therefore, we would like to present here an example of this new type of ionic liquid salt and its application in reactions involving medium and strong bases.

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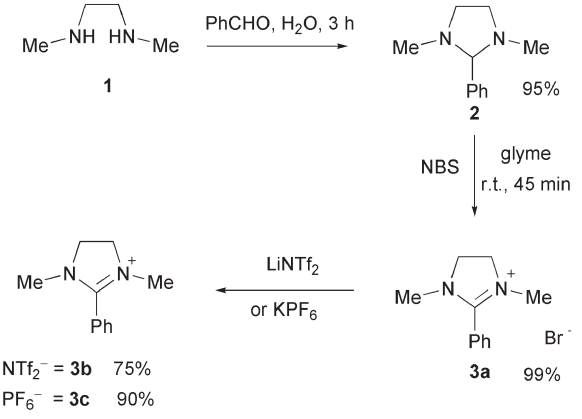
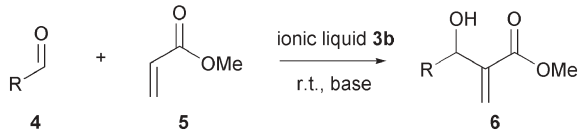
Results and discussion

In order to prepare the salt (Scheme 1), aminal **2** was synthesised according to a literature procedure from diamine **1** and benzaldehyde (**4a**) in water in 95% yield.[15] Compound **2** was oxidised with NBS to the corresponding imidazolinium bromide salt **3a** in 99% yield. Comparatively cheap NBS was chosen as the oxidation reagent instead of NBA (*N*-bromoacetamide), which is often the superior reagent since the product can be purified more easily. Nevertheless, no contamination by succinamide could be detected in the final product. **3a** was hygroscopic and was transformed into the salts **3b** and **3c** by vigorously stirring in the presence of $LiNTf_2$ or KPF_6 in a mixture of water and chloroform for 1 hour. After the aqueous phase had been removed, the chloroform phase was washed three times with water and dried over molecular sieves to furnish the salts **3b** and **3c** in 75% and 90% yield, respectively. The new salts were not hygroscopic. In one run 15 g of salt **3b** was prepared. In the procedure, chloroform can also be replaced with ethyl acetate without decreasing the yield and purity of the product. While **3c** had a melting point of 105 °C, the salt **3b** was a liquid at room temperature. The water content of **3b** was 0.065%, while the bromide impurity was 0.13%, which is comparable with commercially available ionic liquids. Spectral NMR data and CHN analysis demonstrated the purity of the salt. Only after some days did it



Scheme 1



Scheme 2

Table 1 Baylis–Hillman reaction with methyl acrylate[a]

Run	Aldehyde	Base	Time[b]/h	Product	Yield[c] (%)
1	R = Ph, **4a**	DABCO[d]	72	**6a**	53
2	**4a**	Quinuclidinol[d]	24	**6a**	41
3	**4a**	Quinuclidine[d]	48	**6a**	66
4	R = 4-Cl-C_6H_4, **4b**	Quinuclidinol[d]	48	**6b**	52
5	**4b**	Quinuclidine[d]	48	**6b**	66
6	R = 2-C_5H_4N, **4c**	Quinuclidine[d]	48	**6c**	69
7	R = 4-MeO-C_6H_4, **4d**	Quinuclidine[d]	48	**6d**	38
8	R = $PhCH_2CH_2$, **4e**	Quinuclidine[d]	48	**6e**	44
9	**4a**	Quinuclidine[e]	48	**6a**	52
10	**4b**	Quinuclidine[e]	48	**6b**	52
11	**4a**	Quinuclidine[f]	48	**6a**	Traces
12	**4a**	—	48	**6a**	0

[a] 1 equiv. **4**, 1.5 equiv **5**, **3b** (0.4 mL); for a complete procedure see experimental section. [b] Reaction times were not optimised. [c] Isolated yields after column chromatography. [d] 1 equiv. [e] 10 mol%. [f] 1 mol%.

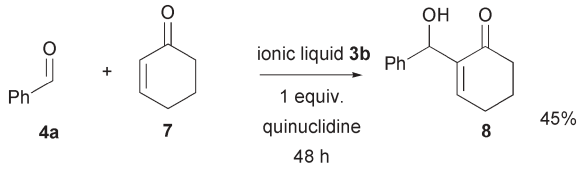
crystallize and a melting point of 35 °C was detected. Prior to use it was melted and it remained a liquid for several hours at room temperature. In the reaction mixture it remained permanently a liquid.

First, salt **3b** was tested as a solvent in the Baylis–Hillman reaction with methyl acrylate (**5**) and various aldehydes (Scheme 2). The results are shown in Table 1. When 1 equiv. of DABCO was used as a catalyst, benzaldehyde (**4a**) and methyl acrylate (**5**) formed the desired product **6a** in 53% yield after 72 h (Table 1, Run 1). Switching to quinuclidinol, the product **6a** was isolated at 52% yield after 24 h, while use of quinuclidine led, in 48 h, to a yield of 66% (Table 1, Runs 2 and 3). With the electron deficient 4-chlorobenzaldehyde (**4b**) and quinuclidinol a yield of 52% after 48 h was achieved, while with quinuclidine 66% was isolated (Table 1 Runs 4 and 5). 2-Pyridinecarbaldehyde (**4c**) gave a yield of 69% after 48 h (Table 1, Run 6). With the electron rich 4-methoxybenzaldehyde (**4c**) and quinuclidine, a yield of 38% was found (Table 1, Run 6). The aliphatic aldehyde, 3-phenylpropionaldehyde (**4d**), gave a yield of 44%. A repeat of the reaction with benzaldehyde and only 10 mol% of quinuclidine gave a slightly lower yield of 52% compared with 1 equiv. of the base (Table 1, Run 9). Aldehyde **4b** yielded, with 10 mol% quinuclidine, the product **6b** at 52% (Table 1, Run 10). However, when only 1 mol% of quinuclidine was used, just traces of the product were isolated after 48 h (Table 1, Run 11). In a control reaction with the absence of base, no product formation could be detected (Table 1, Run 12). The reaction times were not optimized and before the workup, unreacted starting material was still present in the reaction mixture. The ionic liquid was recovered in 93% yield and could be re-used after the work up with no changes in the reactivity: NMR data proved the purity of **3b**. Use of this recovered ionic liquid led to the same yield in the reaction of **4a** with **5**.

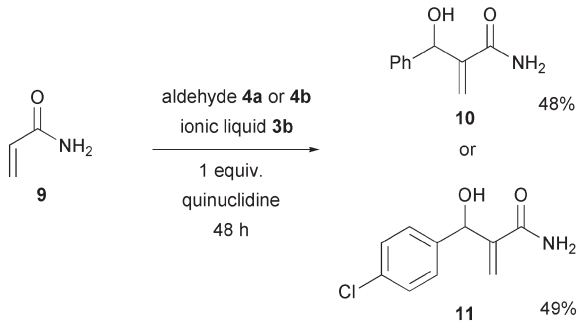
In addition, 2-cyclohexen-1-one (**7**) was applied in a reaction with benzaldehyde (**4a**) in the ionic liquid **3b** with quinuclidine and product **8** was isolated in 45% yield after 48 h (Scheme 3).

Moreover, the behaviour of acrylamide (**9**), which is best soluble in polar solvents, was tested in the reaction as shown in Scheme 4. When acrylamide (**9**) was treated in the ionic liquid **3b** with 1 equiv. of quinuclidine and benzaldehyde (**4a**) the product **10** was isolated in 48% yield after 48 h. The application of 4-chlorobenzaldehyde (**4b**) in the reaction led to the isolated product **11** in 48% yield. The last case is an example in which all reactants were solids, and were all dissolved in the ionic liquid.

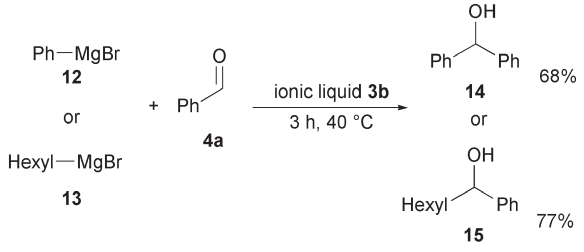
Next, we were interested to see if **3b** would be also suitable as a solvent in reactions involving Grignard reagents, as shown in Scheme 5. Therefore, 3 equiv. of **12** or **13** were placed in a dry vessel and the solvents were evaporated under high vacuum. 2 equiv. of **3b** (0.6 mL) were added in each case and it was observed that the Grignard reagents were dissolved in the ionic liquid. 1 equiv. of benzaldehyde was added and after 3 h at 40 °C, the desired products **14** and **15** were isolated at 68% and 77%, respectively. The ionic liquid was recovered after the workup in 93% yield and NMR data proved the purity of the recovered compound. The reaction temperature of 40 °C was chosen to compare with the standard procedure of adding Grignard reagents to aldehydes in refluxing diethyl ether.[16,17] When recovered ionic liquid was used in the



Scheme 3



Scheme 4



Scheme 5

Grignard reactions, the same yields were obtained with **12** and **13**. During the work up, a triphasic system (hexane, water, ionic liquid) was observed. When **12** was replaced with phenyl lithium, a complex mixture was isolated and no product was detected.

In order to prove the absence of any possible deprotonation in the ionic liquid **3b**, the reaction was repeated with **13**, lacking the addition of benzaldehyde, and after 1 h the mixture was quenched with deuterium oxide. A ^{1}H-NMR spectrum proved the absence of a possible deprotonation. In a second run **13** was replaced with LDA, which led to a complex mixture of compounds.

Conclusions

In conclusion, we have presented a novel ionic liquid based on a 1,3-dimethyl-2-phenylimidazolinium cation. The salt can be used in reactions involving strong bases. The preparation of analogues of these cations should be easy in order to tune the behaviour of these salts, including chiral analogues. A few limits for the ionic liquid in some other applications may be possible. The ionic liquid presented starts to degrade at −1 V measured against ferrocene/ferrocinium, which makes it less suitable for electrochemical applications.[18] Due to the incorporation of an arene ring in the salt, its use in aromatic nitrations[19] might be limited.

Experimental

General experimental

DABCO was purchased from Merck and was used without further purification. Quinuclidine and quinuclidinol were purchased from Fluka and used without further purification. Anhydrous glyme, $LiN(CF_3SO_2)_2$, hexylmagnesium bromide (2 M solution in Et_2O) and phenylmagnesium bromide (1 M solution in THF) were purchased from Aldrich. Benzaldehyde was distilled prior to use. All other reagents were purchased from commercial sources and used without further purification.

Chromatography was performed on a Buechi Sepacore system, using unmodified silica gel as a stationary phase. All reactions were monitored by TLC with Merck Silica gel 60 F_{254} plates. Elemental analyses were carried out by the Microanalytical Laboratory of the Institut für Pharmazeutische Chemie der Universität Braunschweig. Infrared spectra were recorded on a PerkinElmer 2000 FT-IR System. NMR spectra were performed at ambient temperature on a Bruker AC 200F. Mass spectra were recorded on Hewlett–Packard 5898B (at 70 eV). Melting points were taken with an apparatus after the design of Dr. Tottoli and are uncorrected. Water content was determined *via* the Karl Fischer method and bromide content *via* anion chromatography. The two measurements were carried out by the company IoLiTec.

1,3-Dimethyl-2-phenylimidazolidine (2). *N,N*-Dimethylethylenediamine (**1**) (4.15 g, 46.16 mmol) and benzaldehyde (**4a**) (4.90 g, 4.67 mL, 46.16 mmol) were added to a reaction flask filled with water (60 mL). The reaction mixture was vigorously stirred at r.t. for 3 h. The mixture was extracted with $CHCl_3$ (3 × 30 mL) and the combined organic layers were dried (Na_2SO_4). The solvent was distilled off under reduced pressure and the crude product was distilled under reduced pressure, giving the 1,3-dimethyl-2-phenylimidazolidine (**2**) as a colorless liquid (7.71 g, 95%). Spectral data were consistent with literature values.[20]

1,3-Dimethyl-2-phenylimidazolinium bromide (3a). 1,3-Dimethyl-2-phenylimidazolidine (**2**) (7.71 g, 43.74 mmol) was dissolved in glyme (40 mL) and NBS (7.79 g, 43.74 mmol) was added in two portions with an interval of 15 min. An exothermic reaction was observed. After addition of the second portion, the reaction mixture was stirred at r.t. for 30 min and then Et_2O (50 mL) was added in order to precipitate the bromide salt. The solvent was decanted and the oily product was washed with Et_2O (20 mL). The salt was dried *in vacuo*, giving the 1,3-dimethyl-2-phenylimidazolinium bromide (**3a**) as a yellow oil (11.15 g, 99%). This was used directly in the subsequent step. Hygroscopic. ESI-MS: *m/z* 175.1 (cation); IR(KBr) 3417 s, 1710 s, 1616 vs, 1576 m, 1353 m, 1302 m, 1183s cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$) 7.80–7.60 (m, 5 H), 4.32 (s, 4 H), 3.06 (s, 6 H); ^{13}C-NMR (50 MHz, $CDCl_3$) 166.3 (C-2), 132.7, 129.7, 128.7, 121.7, 50.8, 35.0.

1,3-Dimethyl-2-phenylimidazolinium bis(trifluoromethyl-sulfonyl)imide (3b). 1,3-Dimethyl-2-phenylimidazolinium bromide (**3a**) (11.16 g, 43.74 mmol) was dissolved in $CHCl_3$ (10 mL) and it was vigorously stirred with a solution of $LiNTf_2$ (13.81 g, 48.11 mmol) in water (10 mL) for 1 h. The organic layer was washed with a saturated solution of $Na_2S_2O_3$ (20 mL), water (3 × 20 mL) and dried over molar sieves (3Å). The solvent was evaporated, giving the 1,3-dimethyl-2-(phenyl)imidazolinium bis(trifluoromethyl-sulfonyl)imide (**3b**) as a colourless liquid (15 g, 75%) which solidified after a couple of days. m.p. 35 °C; ESI-MS: *m/z* 175.1 (cation); IR (KBr) 1623s, 1578s, 1357vs, 1180vs, 1051vs, 773s, 707s, 614vs 570s, 516s cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$) 7.61–7.49 (m, 5 H, H-Ar), 4.11 (s, 4 H, CH_2–CH_2), 2.96 (s, 6 H, H-Me); ^{13}C-NMR (50 MHz, $CDCl_3$) 166.3, 133.0, 129.8, 128.3, 121.4, 119.9 (q, J = 319.3 Hz), 50.1, 34.5. Formula mass 455.39. Calculated for $C_{13}H_{15}F_6N_3O_4S_2$: C, 34.29; H, 3.32; N, 9.23%; found: C, 34.26, N, 9.14, H, 3.40%. The water content of **3b** was 0.065%, while the bromide impurity was 0.13%.

1,3-Dimethyl-2-phenylimidazolinium hexafluorophosphate (3c). 1,3-Dimethyl-2-(phenyl)imidazolinium bromide (**3a**) (4.27 g, 16.72 mmol) was dissolved in $CHCl_3$ (10 mL) and vigorously stirred with a solution of KPF_6 (3.10 g, 16.72 mmol) in water (5 mL) for 1 h. The organic layer was washed with a saturated solution of $Na_2S_2O_3$ (10 mL), water (3 × 10 mL) and dried over molar sieves (3 Å). The solvent was evaporated, giving the 1,3-dimethyl-2-phenylimidazolinium hexafluorophosphate (**3c**) as a white solid (2.16 g, 90%). m.p. 105 °C; ESI-MS: *m/z* 175.1 (cation); IR (KBr) 3426s, 1623s, 835vs, 557s cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$) 7.70–8.40 (m, 5 H), 4.03 (s, 4 H), 2.86 (s, 6 H); ^{13}C-NMR (50 MHz, $CDCl_3$) 165.1, 131.8, 128.8, 127.3, 120.8, 49.1, 33.4.

General procedure for Baylis–Hillman reaction in ionic liquid. The amine catalyst (1 mmol) was placed in a dry Schlenk flask and ionic liquid **3b** (400 μL, *ca*. 600 mg) was added. An aldehyde (1 mmol) and methyl acrylate (**5**) (135 μL, 1.5 mmol, 1.5 equiv.) were added sequentially. The reaction was stirred at r.t. for 48 h. The reaction mixture was extracted with Et_2O (4 × 5 mL) and the combined ether fractions were evaporated. The crude product was purified by FCC (petrol ether/ethyl acetate, 95/5), giving the desired product.

Regeneration of ionic liquid. The remaining ionic liquid after the extraction was dissolved in $CHCl_3$ (5 mL), washed with 0.5 M HCl (5 mL), water (3 × 5 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure. The ionic liquid was further dried *in vacuo*, giving 1,3-dimethyl-2-(phenyl)-imidazolinium bis(trifluoromethylsulfonyl)imide (**3b**) (470 mg, 78%), The NMR data were identical with the reference sample **3b**. Additional ionic liquid (80 mg, 15%) was obtained from the flash column chromatography by elution with DCM–MeOH (95/5) after separating the Baylis–Hillman product.

Methyl 2-[hydroxy(phenyl)methyl]acrylate (6a). From benzaldehyde (**4a**) (102 μL, 1 mmol), methyl acrylate (**5**) (135 μL, 1.5 mmol) and quinuclidine (115 mg, 1 mmol) in ionic liquid **3b** (400 μL) as colorless oil (127 mg, 66%). Spectral data were consistent with literature values.[21]

Methyl 2-[(4-chlorophenyl)(hydroxy)methyl]acrylate (6b). From 4-chlorobenzaldehyde (**4b**) (145 mg, 1 mmol), methyl acrylate (**5**) (135 μL, 1.5 mmol) and quinuclidine (115 mg, 1 mmol) in ionic liquid **3b** (400 μL) as colorless oil (127 mg, 66%). Spectral data were consistent with literature values.[22]

Methyl 2-[hydroxy(pyridin-2-yl)methyl]acrylate (6c). From 2-pyridinecarbaldehyde (**4c**) (96 μL, 1 mmol), methyl acrylate (**5**) (135 μL, 1.5 mmol) and quinuclidine (115 mg, 1 mmol) in ionic liquid **3b** (400 μL) as colorless oil (133 mg, 69%). Spectral data were consistent with literature values.[23]

Methyl 2-[(4-methoxyphenyl)(hydroxy)methyl]acrylate (6d). From 4-methoxybenzaldehyde (**4d**) (122 μL, 1 mmol), methyl acrylate (**5**) (135 μL, 1.5 mmol) and quinuclidine (115 mg, 1 mmol) in ionic liquid **3b** (400 μL) as colorless oil (84 mg, 38%). Spectral data were consistent with literature values.[21]

Methyl 3-hydroxy-2-methylene-5-phenylpentanoate (6e). From phenylpropionaldehyde (**4e**) (137 μL, 1 mmol), methyl acrylate (**5**) (135 μL, 1.5 mmol) and quinuclidine (115 mg, 1 mmol) in ionic liquid **3b** (400 μL) as colorless oil (97 mg, 44%). Spectral data were consistent with literature values.[24]

2-[Hydroxy(phenyl)methyl]cyclohex-2-enone (8). From benzaldehyde (**4a**) (102 μL, 1 mmol), 1-cyclohexen-2-one (**7**) (147 μL, 1.5 mmol), ionic liquid **3b** (400 μL) and quinuclidine (115 mg, 1 mmol) as colorless oil (92 mg, 46%). Spectral data were consistent with literature values.[25]

2-[Hydroxy(phenyl)methyl]acrylamide (10). From benzaldehyde (**4a**) (102 μL, 1 mmol), acrylamide (**9**) (106 mg, 1.5 mmol) and quinuclidine (115 mg, 1 mmol) in ionic liquid **3b** (400 μL) as a white solid (85 mg, 48%). Spectral data were consistent with literature values.[26]

2-[(4-Chlorophenyl)(hydroxy)methyl]acrylamide (11). From 4-chlorobenzaldehyde (**4b**) (145 mg, 1 mmol) and acrylamide (**9**) (106 mg, 1.5 mmol) and quinuclidine (115 mg, 1 mmol) in ionic liquid **3b** (400 μL) as a white solid (105 mg, 49%). m.p. 111–112 °C, MS (EI), *m*/*z* 210 ($M^+ - H$, 40%), 166 (40), 139 (95), 77 (100), 71 (50), 55 (60); IR (KBr) 3385vs, 3189s, 1658vs, 1624s, 1604s, 1491m, 1198m, 606m cm^{-1}; ^{1}H-NMR (200 MHz, DMSO) 7.47 (s, 1 H) 7.39–7.28 (m, 4 H, H-Ar), 7.01 (s, 1 H), 5.82–5.77 (m, 2 H), 5.62–5.60 (m, 1 H), 5.50–5.48 (m, 1 H); ^{13}C-NMR (50 MHz, DMSO) 168.4, 147.0, 142.3, 131.4, 128.5, 127.8, 117.5, 70.3; HRMS (EI) calculated for $C_{10}H_{10}NO_2ClNa$ 234.0297, found 234.0292.

General procedure for Grignard addition to carbonyl compound in ionic liquid. Commercially available Grignard compound (phenylmagnesium bromide (1 M in THF) or hexylmagnesium bromide (2 M in Et_2O) (3 mmol) was placed in a dry Schlenk flask under nitrogen and the solvent was removed *in vacuo*. Ionic liquid **3b** (600 mL, *ca*. 900 mg) was added and the reaction mixture formed a clear solution. Benzaldehyde (101 μL, 1 mmol) was added at once. The reaction mixture warmed up spontaneously. After the exothermic reaction ended, the reaction mixture was heated up to 40 °C for 3 h. The reaction mixture was quenched with saturated solution of NH_4Cl and extracted with hexane (4 × 10 mL). The combined organic layers were dried (Na_2SO_4) and the solvent was distilled off under reduced pressure. The crude product was purified by FCC (petroleum ether–ethyl acetate, 95/5), giving the corresponding alcohol.

Regeneration of ionic liquid. The ionic liquid remained after extraction with hexane as a phase below the aqueous phase. It was dissolved in $CHCl_3$ (5 mL), washed with water (3 × 5 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure and the ionic liquid was further dried *in vacuo*, giving 1,3-dimethyl-2-phenylimidazolinium bis(trifluoromethylsulfonyl)imide (**3b**) (837 mg, 93%), NMR data were identical with the reference sample **3b**.

Diphenylmethanol (14). From phenylmagnesium bromide (**12**) (3 ml 1 M THF solution, 3 mmol) and benzaldehyde (**4a**) (102 μL, 1 mmol) in ionic liquid **3b** (600 μL) as a white solid (125 mg, 68%). Spectral data were consistent with literature values.[27]

1-Phenylheptan-1-ol (15). From hexylmagnesium bromide (**13**) (1.5 mL 2 M Et_2O solution, 3 mmol) and benzaldehyde (**4a**) (102 μL, 1 mmol) in ionic liquid **3b** (600 μL) as a colorless oil (150 mg, 77%). Spectral data were consistent with literature values.[28]

Deuterium exchange experiment using ionic liquid and hexylmagnesium bromide. Hexylmagnesium bromide (**13**) (1 mL, 2 mmol) was placed in a Schlenk flask and the solvent was evaporated *in vacuo*. Ionic liquid **3b** (300 mg, 0.75 mmol)

was added and the reaction mixture stirred at 40 °C for 1 hour before being quenched by addition of D_2O. The ionic liquid was separated from the aqueous phase and dissolved in $CHCl_3$. The organic phase was washed with water (3 × 3 mL), dried (Na_2SO_4) and the solvent was removed under reduced pressure. The ionic liquid was dried *in vacuo*. ^{1}H-NMR was recorded and shown to be identical with the original sample of **3b**.

Acknowledgements

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New chiral ionic liquids based on imidazolinium salts

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ABSTRACT

The preparation and application of a new series of chiral ionic liquids are described. The salts are based on imidazolinium cations. Some of the cations also incorporated an axial chirality at the C(2) position next to the central chirality. These cations display a very high rotational barrier along the arene–imidazolinium axis. Furthermore, an analogue with a chiral anion was prepared. The salts have low melting points. Their potential as solvents and as chiral shift reagents was explored, resulting for the first time in an example of a chiral ionic liquid as a shift reagent for a neutral compound.

1. Introduction

Over the years, ionic liquids and salts with a melting point below 100 °C have proven to be a promising class of organic materials due to their potential as novel solvents for reactions and electrochemical processes.[1] Many of these liquids could be potential 'green solvents', due to their negligible vapor pressure or efficient recovery.[2] However, a few studies have been reported that show that ionic liquids are not inert but do react with some reagents,[3,4] which could be a disadvantage in some applications, for example, in recovery. Imidazolium cations are most frequently applied in many standard ionic liquids. These cations can be deprotonated with medium and strong bases.[5–9] Therefore, a number of alternative ionic liquids have recently been reported, which can be used in the presence of basic Grignard reagents.[10–15] The first example, reported by Clyburne et al.,[10] was a phosphonium ionic liquid. Thereafter, we reported the application of an imidazolinium salt.[11]

Handy reported that an *i*Pr group at the C-2 position of an imidazolium cation leads to a base-stable imidazolium RTIL for the Grignard addition to aldehydes.[13] In addition, Chan et al.[12] reported the application of *n*-butylpyridinium tetrafluoroborate in this reaction. It was also possible to prepare the Grignard reagent in this ionic liquid. In addition, Itho reported the use of salts based on phosphonium cations with alkyl ether side arms for the Grignard addition to aldehydes.[15]

If ionic liquids are chiral, they have an additional potential as chiral solvents, shift reagents, and catalysts.[16–31] Most of these chiral ionic liquids incorporate a central chirality and only a few are known based on planar[28] and axial chirality.[30] Chiral ionic liquids based on imidazolinium salts can have a stereogenic center at the C(4) or C(5) position, and it is known that no racemization occurs at these positions.[31] Due to our efforts on the chiral ionic liquids,[32–36] we were interested in preparing chiral analogues of imidazolinium salts incorporating ether functions with a different chiral environment and an aryl substituent at the C(2) position, which would also allow the introduction of an axial chirality. The salts were investigated as solvents in the Grignard addition to aldehydes and as chiral shift reagents.

2. Results and discussion

The synthesis of chiral ionic liquids is shown in Scheme 1. First L-valinol[37] **1a** was reacted with either benzoyl- or *o*-toluoyl chloride in the presence of potassium carbonate in methanol.[38] The corresponding amides could be obtained as white solids in 73% yield for **2a** and 95% yield for **2b**, respectively. Furthermore, the achiral *N*-benzoylethylamine **2c** and *N*-(2-hydroxyethyl)-2-methylbenzamide **2d** were obtained from ethanolamine **1b** and benzoyl chloride or toluoyl chloride in 93% and 71% yield, respectively.

These amides were then treated with neat thionyl chloride and subsequently with aqueous methylamine to give the desired 1-methylimidazolines. (*S*)-4-Isopropyl-1-methyl-2-phenyl-4,5-dihydro-1*H*-imidazole **3a** was isolated in 82% yield, whereas (*S*)-4-isopropyl-1-methyl-2-*o*-tolyl-4,5-dihydro-1*H*-imidazole **3b** was obtained only in 47% yield probably due to increased steric hindrance during the reaction with thionyl chloride. 1-Methyl-phenyl-4,5-dihydro-1*H*-imidazole **3c** was obtained as a colorless liquid in 77% yield, whereas 1-methyl-2-*o*-tolyl-4,5-dihydro-1*H*-imidazole **3d** was obtained in 67% yield.

The prepared 4,5-dihydro-1*H*-imidazoles **3a–d** were afterwards subjected to nucleophilic substitution reactions with electrophiles containing ether moieties, namely MOM-chloride, MEM-chloride, and (−)-menthyl chloride. (−)-Menthyl chloride was prepared via the standard procedure from menthol, paraformaldehyde, and hydrochloric acid.[39] The chlorides obtained were directly dissolved in water and the addition of $LiNTf_2$ led to the precipitation of the chiral ionic liquids. Depending on the synthetic route, the final

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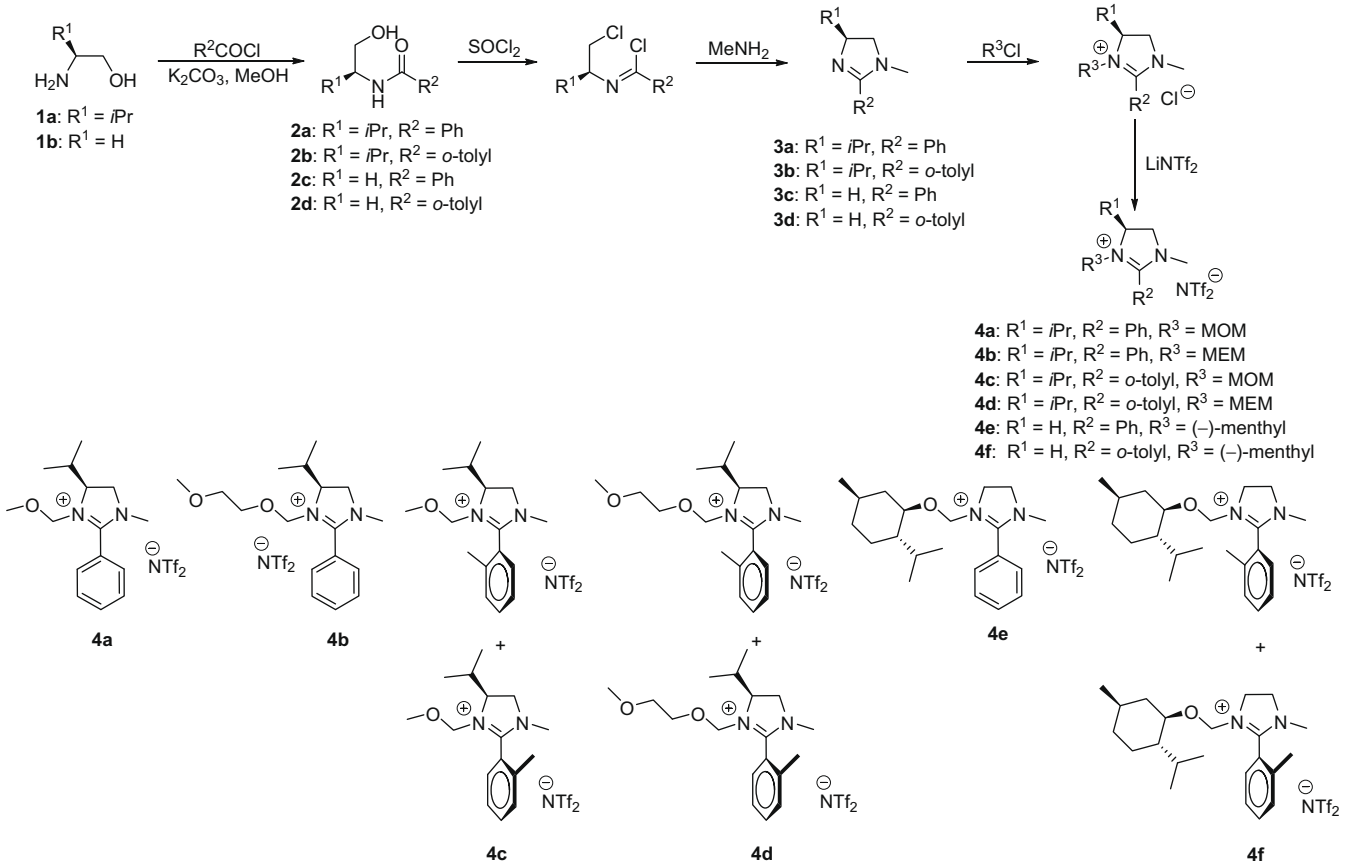


Scheme 1. Synthesis of chiral ionic liquids.

cation carried the chiral information directly at the imidazolium ring or at the imidazoline nitrogen atom.

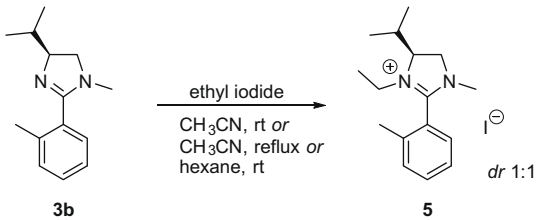
All the salts prepared are ionic liquids, respectively, with melting points at 39 °C, **4a**; 44 °C, **4c;** and 58 °C, **4e** or are room-temperature ionic liquids at 20 °C, **4b**, **4d**, and **4f**.

The ionic liquids, which have an *o*-tolyl group at the C2-position of the imidazolinium ring, also have next to an element of central chirality an element of axial chirality. The rotation around the axis is hindered, which makes it possible to observe in the NMR separate signals for each diastereomer. Scheme 1 shows the different diastereomers of the ionic liquids bearing additional axial chirality.

The diastereomeric ratios for the described ionic liquids were calculated from the ^{1}H NMR data. The following ratios were observed: 3:2, **4c;** 4:3, **4d;** and 1:1, **4f**. It was not possible to separate the diastereomers with any of the several standard methods or with HPLC with normal or reversed phase. The assignment of the peaks to a specific diastereomer was not possible by NOE. However, it is reasonable to assume for **4c** and **4d** that the less sterically demanding diastereomer is formed in excess.

While free rotation in salts **4c**, **4d,** and **4f** is restricted, there is no rotational barrier in the corresponding imidazolines **3c**, **3d,** and **3f**. The tolyl group is locked in the quaternization process and an obviously high rotation barrier prevents free rotation around the C2–C(tolyl) axis because of steric hindrance between the newly introduced substituent at the C1-carbon and the methyl group of the tolyl ring. In order to determine the rotational barrier, IL **4c** was heated in DMSO-d_6 during the NMR measurement from rt to 50, 100, and 150 °C in order to evaluate any changes in the diastereomeric ratio. However, even at 150 °C, no change in the NMR was observed meaning that one can assume a high rotational barrier around the imidazolinium–tolyl C–C axis.

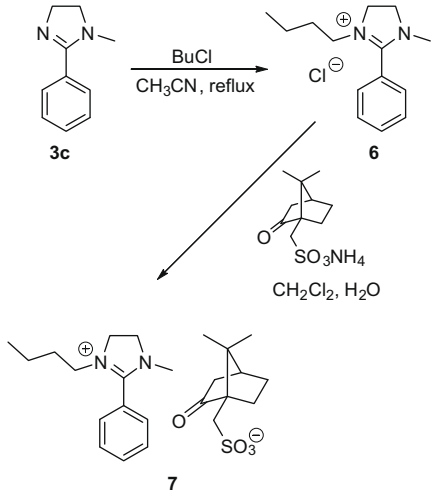
To explore whether the reaction temperature of the quaternization step would have an influence on the diastereomeric ratio of the product, imidazoline **3b** was reacted with ethyliodide in acetonitrile at rt and at reflux. In addition, acetonitrile was replaced with hexane and the reaction was carried out at rt to investigate the influence of the solvent (Scheme 2). From the obtained NMR data, in all cases, a diastereomeric ratio of ~1:1 was obtained.



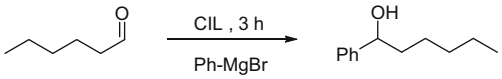
Scheme 2. Synthesis of salt **5**.

An imidazolinium salt was prepared with a chiral anion based on (−)-camphorsulfonic acid as shown in Scheme 3. The precursor **3c** was treated with butyl chloride in refluxing acetonitrile to give the desired product **6** in 65% yield. Subsequent anion metathesis with commercially available (−)-ammonium camphorsulfonate gave the new rt chiral ionic liquid **7** in 86% yield.

The ionic liquids **4a**–**f** were tested in the Grignard addition to aldehydes (Scheme 4). The THF solvent of the commercial Grignard solution was evaporated under high vacuum and the ionic liquid was added to the remaining solid Grignard. After heating to



Scheme 3. Synthesis of salt **7**.



Scheme 4. Grignard addition to aldehydes.

40 °C, the aldehyde was added and the reaction mixture was stirred for 3 h.

Ionic liquids **4e** and **4f** gave the desired product in yields comparable to an achiral analogue.[11] Since ionic liquid **4e** gave the highest yield, the addition of phenylmagnesiumbromide to 1-naphthaldehyde was also tested herein. The corresponding product was isolated in 52% yield. In all the reactions, no optical activity was found. Two reactions were carried out in the presence of a Lewis acid and **4a** as a solvent. Moreover, 10 mol % of the Lewis acids, zinc chloride or scandium triflate, was used. However, the yields decreased to 30% with zinc chloride and to 20% with scandium triflate.

Next, the behavior of the salts as chiral shift reagents was tested with enantiomerically and diastereomerically pure ionic liquids **4a**, **4b**, and **4e**, and with ionic liquid **7**. For the NMR measurements, racemic Mosher's acid potassium salt with 18-crown-6 or 1-phenyl-2,2,2-trifluoroethanol was used. In a typical NMR experiment, the CIL/substrate ratio was 2:1. With **4a** and **4b**, racemic potassium Mosher's carboxylate and 18-crown-6, a splitting of 15.14 Hz and 5.17 Hz in the ^{19}F NMR was observed when $CDCl_3$ was used as a solvent. In the ^{1}H NMR no splitting was found. With salt **4e** no splitting was observed in either the ^{1}H or ^{19}F NMR.

In order to evaluate salt **7**, Mosheŕs acid was added to the salt in toluene-d_8. However, no splitting was observed. Next (±)-1-phenyl-2,2,2-trifluoroethanol with **7** in $CDCl_3$ showed no splitting of the C1-proton of the alcohol, but a downfield shift of 0.2 ppm was observed. The results changed drastically when toluene-d_8 was used as the solvent. The alcohol's C1-proton signal was shifted from 4.38 ppm (without ionic liquid) to 5.62 ppm. Also a splitting of the quadruplet was observed. The chiral recognition by ionic liquid **7** caused a splitting of about 2.5 Hz in the ^{1}H NMR. However, in some cases, a splitting of the quadruplet signal was observed although no ionic liquid was applied. This was due to the fact that the decreased humidity of the reagents and solvents used in the experiments caused a further coupling of the CH-proton of the alcohol with the hydroxyl proton. To exclude this influence in determining the splitting, enantiomerically enriched 1-phenyl-2,2,2-trifluoroethanol [(*S*)-enriched, 50% ee and 33% ee] was applied. In the ^{19}F NMR, the splitting of the CF_3 doublet was 6.9 Hz as shown in Figure 1.

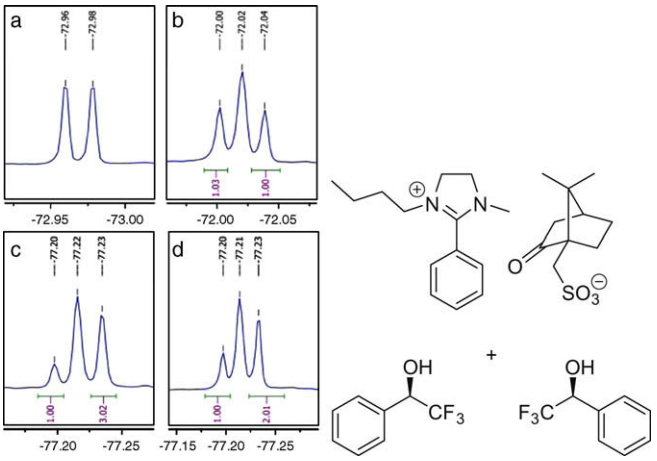


Figure 1. (a) (±)-1-Phenyl-2,2,2-trifluoroethanol in toluene-d_8, (b) (±)-1-phenyl-2,2,2-trifluoroethanol (1 equiv) + **7** (2 equiv) in toluene-d_8, 1-phenyl-2,2,2-trifluoroethanol [50% ee, (*S*)-enriched, 1 equiv] + **7** (2 equiv) in toluene-d_8, (c) 1-phenyl-2,2,2-trifluoroethanol [33% ee, (*S*)-enriched, 1 equiv] + **7** (2 equiv) in toluene-d_8.

3. Conclusion

In conclusion, it was possible to synthesize a series of chiral ionic liquids containing ether functions of which some incorporated axial chirality. In the future, analogues with larger groups in the backbone of the imidazolinium ring and at the *ortho* position of the aryl substituent will be prepared in order to increase the diastereoselectivity. While the ionic liquids did not induce any asymmetric excess in the addition of Grignard reagent to aldehydes, it was possible to show that they are able to form diastereomeric salt pairs with Mosher's carboxylates. More importantly, it was possible to show that a salt with a chiral camphor sulfonate anion can be used as a chiral shift reagent for a neutral alcohol.

4. Experimental

4.1. General experimental

Toluene was dried over sodium. L-Valinol **1a**[37] was prepared according to the literature. Flash column chromatography[40] was performed on silica gel. All reactions were monitored by TLC plates. ^{1}H NMR spectra were acquired with a Bruker AC 200F (200 MHz) at ambient temperature. Chemical ^{13}C NMR spectra were recorded at ambient temperature with AC 200F (50 MHz) instruments and chemical shifts were reported in parts per million (ppm) relative to tetramethylsilane as the internal standard. NMR samples were dissolved if not otherwise stated in $CDCl_3$. Mass spectra (ESI) were recorded with a Hewlett–Packard MS LC/MSD Series 1100 MSD instrument, while HRMS were recorded on a Bruker Daltonik Tesla-Fourier Transform-Ion Cyclotron Resonance Mass spectrometer mit Electrospray-Ionisierung by Dr. Dräger at the Institute of Organic Chemistry, University of Hannover. Infrared spectra were recorded with a Bruker Vektor 22 FTIR spectrometer, as KBr pellets in case of solid compounds and as thin films between NaCl plates in cases of oils and liquids. HPLC analysis was carried out using a Daicel CHIRALPACK OD-H column with a Waters 510 Pump system, an ISCO Model UA-5 UV–vis Detector (254 nm), and a Waters 410 differential refractometer. Melting points were taken with a Dr. Tottoli apparatus and are uncorrected.

4.2. Preparation of hydroxy-protected bis-hydroxy amines

4.2.1. Preparation of benzamides 2a–2d: General procedure

Potassium carbonate (12.5 g) was suspended in methanol (400 mL). The aminoalcohol **1a** or **1b** (83.1 mmol) was added and the mixture was cooled down to 0 °C. Afterwards, the acid chloride (91.4 mmol) was added and the mixture was stirred for 15 h at rt. The remaining solid was decanted off and the solvent was distilled off. Water (100 mL) and chloroform (200 mL) were added and the mixture was stirred for 15 min. The organic phase was separated, and the aqueous phase was washed with chloroform (3 × 100 mL). The combined organic phases were dried over sodium sulfate. After distilling off the solvent, the remaining solid was washed with a small amount of cold toluene and afterwards dried in high vacuum.

4.2.1.1. (*S*)-*N*-(1-Hydroxy-3-methylbutan-2-yl)-benzamide 2a. As a white solid (73%). ^{1}H NMR (200 MHz) δ 7.91–7.63 (m, 2H), 7.61–7.30 (m, 3H), 6.60 (d, J = 8.3 Hz, 1H), 4.03–3.80 (m, 1H), 3.82–3.64 (m, 2H), 3.19 (s, 1H), 2.19–1.78 (m, 1H), 1.00 (d, J = 3.2 Hz, 3H), 0.97 (d, J = 3.3 Hz, 3H); ^{13}C NMR (50 MHz) δ 168.5, 134.6, 131.6, 128.7, 127.1, 63.6, 57.5, 29.3, 19.7, 19.1. The spectral data were consistent with literature values.[41]

4.2.1.2. (*S*)-*N*-(1-Hydroxy-3-methylbutan-2-yl)-2-methylbenzamid 2b. As a white solid (95%). Mp 89.2 °C; $[\alpha]_D^{25} = -27.8$ (c 0.42, $CHCl_3$); MS (EI), m/e 222 (M^++H, 3%), 136 (11), 119 (100), 91 (42); IR (KBr) 3293, 3069, 2964, 2880, 2360, 1638, 1538, 1463, 1338, 1314, 1068, 1017, 901, 878, 845, 778, 742, 724, 698 cm^{-1}; ^{1}H NMR (200 MHz) δ 7.35–7.02 (m, 4H), 5.99 (d, J = 7.7 Hz, 1H), 3.93–3.75 (m, 1H), 3.74–3.56 (m, 2H), 2.78 (s, 1H), 2.36 (s, 3H), 1.99–1.78 (m, 1H), 0.95 (d, J = 3.3 Hz, 3H), 0.91 (d, J = 3.4 Hz, 3H); ^{13}C NMR (50 MHz) δ 171.2, 136.7, 136.0, 131.1, 130.0, 126.7, 125.9, 64.0, 57.4, 29.2, 19.9, 19.7, 19.0. HRMS (EI): calcd for $C_{13}H_{19}NO_2$ [M$^+$]: 221.1416, found 221.1418.

4.2.1.3. *N*-(2-Hydroxyethyl)-benzamide 2c. As a white solid (93%). ^{1}H NMR (200 MHz) δ 7.85–7.66 (m, 2H), 7.52–7.14 (m, 4H), 4.05 (s, 1H), 3.74 (t, J = 4.9 Hz, 2H), 3.62–3.45 (m, 2H), OH-proton not observed; ^{13}C NMR (50 MHz) δ 168.9, 134.1, 131.7, 128.6, 127.1, 61.8, 42.9. The spectral data were consistent with literature values.[42]

4.2.1.4. *N*-(2-Hydroxyethyl)-2-methylbenzamide 2d. As a white solid (71%). Mp 65 °C; MS (EI), m/e 179 (M^+, 7%), 136 (11), 119 (100), 91 (57), 77 (3); IR (KBr) 3279, 3070, 3025, 2971, 2932, 2884, 1966, 1933, 1816, 1637, 1420, 1315, 1164, 1119, 1095, 1047, 883, 868, 779, 755, 729, 702, 659, 521, 461, 416 cm^{-1}; ^{1}H NMR (200 MHz) δ 7.42–7.06 (m, 4H), 6.48 (s, 1H), 3.83–3.63 (m, 2H), 3.61–3.42 (m, 2H), 3.23 (s, 1H), 2.40 (s, 3H); ^{13}C NMR (50 MHz) δ 171.4, 136.1, 136.0, 131.1, 130.1, 126.9, 125.8, 62.2, 42.7, 19.8. Anal. Calcd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82. Found: C, 66.97; H, 7.38; N, 7.82.

4.2.2. Preparation of imidazolines 3a–3d: General procedure

Hydroxybenzamides **2a**–**2d** (197 mmol) were carefully treated with neat thionyl chloride (0.79 mol). The resulting solution was refluxed for 4 h. The excess of thionyl chloride was distilled off. Dry diethyl ether (200 mL) was added to the remaining oil. The small amount of insoluble solid was filtered off and the filtrate was cooled down to 0 °C. Aqueous methyl amine solution (200 mL, 11.85 M) was added and the resulting mixture was stirred for 1 h at rt. The organic phase was separated, and the aqueous phase was washed with chloroform (3 × 300 mL). The combined organic phases were dried over sodium sulfate. After distilling off the solvent, the remaining oil was purified via bulb-to-bulb distillation.

4.2.2.1. (*S*)-4-Isopropyl-1-methyl-2-phenyl-4,5-dihydro-1*H*-imidazole 3a. As a colorless liquid (82%). $[\alpha]_D^{25} = -84.0$ (c 1.07, $CHCl_3$); MS (EI), m/e 202 (M^+, 3%), 185 (3), 174 (5), 159 (100), 132 (3), 118 (7), 104 (20), 91 (10), 77 (27); IR (NaCl) 3060, 3022, 2955, 2870, 1957, 1895, 1653, 1614, 1597, 1573, 1448, 1383, 1364, 1310, 1264, 1217, 1064, 1026, 971, 945, 923, 778, 702, 588, 544, 433 cm^{-1}; ^{1}H NMR (200 MHz) δ 7.52–7.34 (m, 2H), 7.34–7.18 (m, 3H), 3.77 (ddd, J = 10.4, 9.2, 6.0 Hz, 1H), 3.40 (dd, J = 10.3, 9.2 Hz, 1H), 2.94 (t, J = 9.2 Hz, 1H), 2.63 (s, 3H), 1.89–1.63 (m, 1H), 0.92 (d, J = 6.8 Hz, 3H), 0.83 (d, J = 6.8 Hz, 3H); ^{13}C NMR (50 MHz) δ 166.3, 131.1, 129.2, 127.9 (2C), 70.0, 55.9, 35.8, 32.9, 18.8, 17.8. HRMS (EI): calcd for $C_{13}H_{18}N_2$ [M$^+$]: 202.1470, found 202.1472.

4.2.2.2. (*S*)-4-Isopropyl-1-methyl-2-*o*-tolyl-4,5-dihydro-1*H*-imidazole 3b. As a yellow liquid (47%). $[\alpha]_D^{25} = +58.3$ (c 1.43, $CHCl_3$); MS (EI), m/e 216 (M^+, 18%), 201 (5), 173 (100), 117 (22), 103 (8), 91 (21), 85 (7), 77 (11); IR (NaCl) 3061, 3022, 2955, 2870, 1619, 1597, 1497, 1458, 1382, 1364, 1309, 1262, 1232, 1061, 1040, 944, 771, 732, 588, 532, 446, 436, 428 cm^{-1}; ^{1}H NMR (200 MHz) δ 7.34–7.13 (m, 5H), 3.92 (ddd, J = 10.3, 9.2, 6.0 Hz, 1H), 3.47 (dd, J = 18.3, 9.2 Hz, 1H), 3.08 (t, J = 9.2 Hz, 1H), 2.57 (s, 3H), 2.32 (s, 3H), 1.98–1.74 (m, 1H), 1.03 (d, J = 6.8 Hz, 3H), 0.96 (d, J = 6.8 Hz, 3H); ^{13}C NMR (50 MHz) δ 166.2, 136.3, 131.5, 130.2, 129.1, 128.7, 125.7, 70.7, 55.3, 34.5, 33.2, 19.5, 19.1, 18.4. HRMS (EI): calcd for $C_{14}H_{20}N_2$ [M$^+$]: 216.1626, found 216.1625.

4.2.2.3. 1-Methyl-phenyl-4,5-dihydro-1*H*-imidazole 3c. As a colorless liquid (77%). ^{1}H NMR (200 MHz) δ 7.60–7.45 (m, 2H), 7.46–7.30 (m, 3H), 3.95–3.76 (m, 2H), 3.52–3.33 (m, 2H), 2.78 (s, 3H); ^{13}C NMR (50 MHz) δ 168.1, 131.3, 129.6, 128.2, 128.1, 54.1, 53.2, 36.4. The spectral data were consistent with literature values.[43]

4.2.2.4. 1-Methyl-2-*o*-tolyl-4,5-dihydro-1*H*-imidazole 3d. As a colorless liquid (67%). MS (EI), m/e 173 (88%, [M$^+$]), 159 (67%), 91 (23%), 84 (100%), 77 (28%); IR (NaCl) 3061, 3022, 2926, 2861, 1922, 1720, 1618, 1595, 1496, 1451, 1381, 1327, 1272, 1227, 1182, 1119, 1085, 1057, 1039, 989, 942, 770, 731, 589, 533 cm^{-1}; ^{1}H NMR (200 MHz) δ 7.36–7.13 (m, 4H), 3.98–3.78 (m, 2H), 3.49–3.30 (m, 2H), 2.57 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (50 MHz) δ 167.4, 136.2, 131.4, 130.0, 128.9, 128.3, 125.5, 53.4, 53.0, 34.6, 19.2. HRMS (EI): calcd for $C_{11}H_{14}N_2$ [M$^+$]: 174.1157, found 174.1158.

4.2.3. Synthesis of ionic liquids 4a–4f: General procedure

The particular 4,5-dihydro-1*H*-imidazole (5.2 mmol) was dissolved in dry acetonitrile (3 mL), and the electrophilic chloride [MOM-, MEM-, or (−)-menthyl chloride] was added (10.4 mmol). The solution was refluxed for 15 h. After cooling the solvent the remaining electrophile was distilled off. The remainder was dissolved in water (10 mL), and $LiNTf_2$ (7.8 mmol) in water (5 mL) was added. An organic phase separated immediately. The mixture was stirred for an additional 30 min. The water was decanted off and the ionic liquid was washed three times with water. Dichloromethane was added and the organic phase was dried over sodium sulfate. After distilling off the solvent, the ionic liquids were dried under high vacuum for at least 15 h at 50 °C.

4.2.3.1. (*S*)-4-Isopropyl-3-(methoxymethyl)-1-methyl-2-phenyl-4,5-dihydro-1*H*-imidazol-3-ium bis(trifluoromethylsulfonyl) amide 4a. As an orange solid (77%). Mp 39 °C; $[\alpha]_D^{25} = +20.1$ (c 1.33, $CHCl_3$); MS (EI), m/e 247 ([M$_{cation}$]$^+$, 100%), 203 (29), 159 (21), 118 (8), 77 (6); MS (ESI, 0 V) m/e 247.3 ([M$_{cation}$]$^+$, 100%); IR (KBr) 3320, 2968, 1624, 1604, 1549, 1491, 1467, 1449, 1395, 1353, 1288, 1195, 1137, 1098, 1057, 944, 917, 788, 740, 700, 654, 617 cm^{-1}; ^{1}H NMR (400 MHz) δ 7.81–7.49 (m, 5H), 4.60–

4.17 (m, 4H), 3.72 (dd, *J* = 10.8, 7.2 Hz, 1H), 3.18 (s, 3H), 3.06 (s, 3H), 2.47–2.20 (m, 1H), 1.02 (d, *J* = 0.9 Hz, 3H), 0.98 (d, *J* = 1.3 Hz, 3H); ^{13}C NMR (100 MHz) δ 167.7, 133.8, 130.0, 128.8, 121.1, 120.1 (q, J_{CF} = 321 Hz), 78.1, 64.6, 56.4, 51.8, 34.8, 28.9, 17.7, 14.5. Anal. Calcd for $C_{17}H_{23}F_6N_3O_5S_2$: C, 38.71; H, 4.39; N, 7.97. Found: C, 38.58; H, 4.28; N, 8.04.

4.2.3.2. (*S*)-4-Isopropyl-3-((2-methoxyethoxy)methyl)-1-methyl-2-phenyl-4,5-dihydro-1*H*-imidazol-3-ium bis(trifluoromethylsulfonyl)amide 4b. As a yellow liquid (77%). $[\alpha]_D^{25} = +18.0$ (*c* 1.29, $CHCl_3$); MS (EI), *m/e* 291 ([M_{cation}]$^+$, 100%), 247 (11), 203 (13), 159 (23); MS (ESI, 0 V) *m/e* 290.9 ([M_{cation}]$^+$, 100%); IR (KBr) 3308, 3067, 2968, 2883, 2360 1929, 1623, 1604, 1549, 1491, 1466, 1449, 1352, 1352, 1192, 1136, 1093, 1058, 787, 740, 700, 654, 616, 571, 513, 462, 444, 436 cm^{-1}; ^{1}H NMR (400 MHz) δ 7.78–7.54 (m, 5H), 4.70 (d, *J* = 10.9 Hz, 1H), 4.59 (d, *J* = 10.9 Hz, 1H), 4.49 (ddd, *J* = 12.0, 8.1, 3.6 Hz, 1H), 4.24 (t, *J* = 12.0 Hz, 1H), 3.80 (dd, *J* = 12.0, 8.1 Hz, 1H), 3.56–3.37 (m, 4H), 3.29 (s, 3H), 3.07 (s, 3H), 2.47–2.27 (m, 1H), 1.03 (d, *J* = 1.8, 3H), 1.01 (d, *J* = 2.0 Hz, 3H); ^{13}C NMR (100 MHz) δ 167.3, 133.6, 129.9, 128.7, 120.9, 120.0 (q, J_{CF} = 321 Hz,), 76.3, 71.5, 68.3, 63.6, 58.8, 51.5, 34.6, 28.1, 17.6, 14.2. Anal. Calcd for $C_{19}H_{27}F_6N_3O_6S_2$: C, 39.93; H, 4.76; N, 7.35. Found: C, 40.07; H, 4.76; N, 7.45.

4.2.3.3. (*S*)-4-Isopropyl-3-(methoxymethyl)-1-methyl-2-*o*-tolyl-4,5-dihydro-1*H*-imidazol-3-ium bis(trifluoromethylsul-fonyl)amide (mixture of diastereomers, dr ~ 2:3) 4c. As a yellow solid (73%). MS (EI), *m/e* 261 ([M_{cation}]$^+$, 100%), 246 (2), 218 (13); MS (ESI, 0 V) *m/e* 261.8 ([M_{cation}]$^+$, 100%); IR (KBr) 3306, 2963, 2771, 2683, 2593, 2366, 2194, 2017, 1930, 1847, 1770, 1625, 1550, 1467, 1350, 1284, 1052, 942, 916, 789, 772, 739, 699, 613, 569, 514 cm^{-1}; ^{1}H NMR (400 MHz) (diastereomer 1, 40%) δ 7.66–7.25 (m, 4H), 4.65–4.18 (m, 4H), 3.86 (ddd, *J* = 14.9, 12.1, 8.9 Hz, 1H), 3.18 (s, 3H), 2.98 (s, 3H), 2.43–2.34 (m, 1H), 2.33 (s, 3H), 1.09–0.97 (m, 6H); ^{13}C NMR (100 MHz) (diastereomer 1, 40%) δ 167.8, 137.0, 133.4, 131.7, 128.2, 127.3, 120.5, 119.9 (q, J_{CF} = 321 Hz), 76.9, 64.1, 56.7, 51.3, 34.08, 28.3, 18.8, 17.6, 14.3; ^{1}H NMR (400 MHz) (diastereomer 2, 60%) δ 7.66–7.25 (m, 4H), 4.65–4.18 (m, 4H), 3.86 (ddd, *J* = 14.9, 12.1, 8.9 Hz, 1H), 3.17 (s, 3H), 2.97 (s, 3H), 2.43–2.34 (m, 1H), 2.29 (s, 3H), 1.09–0.97 (m, 6H); ^{13}C NMR (100 MHz) (diastereomer 2, 60%) δ 167.4, 136.3, 133.1, 131.5, 128.3, 127.4, 121.0, 119.9 (q, J_{CF} = 321 Hz), 77.2, 63.8, 56.6, 51.1, 34.13, 27.7, 19.1, 17.8, 14.7. Anal. Calcd for $C_{18}H_{25}F_6N_3O_5S_2$: C, 39.92; H, 4.65; N, 7.76. Found: C, 40.17; H, 4.76; N, 7.73.

4.2.3.4. (*S*)-4-Isopropyl-3-((2-methoxyethoxy)methyl)-1-methyl-2-*o*-tolyl-4,5-dihydro-1*H*-imidazol-3-ium bis(trifluoromethylsulfonyl)amide (mixture of diastereomers, dr ~ 1:1.1) 4d. As a yellow liquid (62%). MS (EI), *m/e* 261 305 ([M_{cation}]$^+$, 100%), 261 (9), 217 (11), 173 (11), 132 (2); MS (ESI, 0 V) *m/e* 305.1 ([M_{cation}]$^+$, 100%); IR (NaCl) 3312, 3067, 2968, 2937, 2883, 2591, 2366, 1931, 1847, 1799, 1623, 1604, 1550, 1465, 1352, 1287, 1190, 1135, 1057, 985, 942, 890, 850, 788, 769, 7,39, 655, 617, 571, 513 cm^{-1}; ^{1}H NMR (400 MHz) (diastereomer 1, 48%) δ 7.65–7.22 (m, 4H), 4.75–4.38 (m, 3H), 4.36–4.14 (m, 1H), 3.83 (dd, *J* = 20.6, 10.6 Hz, 1H), 3.57–3.28 (m, 4H), 3.24 (s, 3H), 2.97 (s, 3H), 2.45–2.34 (m, 1H), 2.33 (s, 3H), 1.11–0.92 (m, 6H); ^{13}C NMR (100 MHz) (diastereomer 1, 48%) δ 167.9, 137.3, 133.4, 131.85, 128.2, 127.4, 120.7, 119.9 (q, J_{CF} = 321 Hz), 76.1, 71.8, 68.7, 63.8, 58.9, 51.4, 34.2, 28.2, 18.9, 17.7, 14.4; ^{1}H NMR (400 MHz) (diastereomer 2, 52%) δ 7.65–7.22 (m, 4H), 4.75–4.38 (m, 3H), 4.36–4.14 (m, 1H), 3.83 (dd, *J* = 20.6, 10.6 Hz, 1H), 3.57–3.28 (m, 4H), 3.25 (s, 3H), 2.96 (s, 3H), 2.45–2.34 (m, 1H), 2.26 (s, 3H), 1.11–0.92 (m, 6H); ^{13}C NMR (100 MHz) (diastereomer 2, 52%) δ 167.4, 136.2, 133.2, 131.5, 128.5, 127.6, 121.0, 119.9 (q, J_{CF} = 321 Hz), 75.8, 71.6, 68.6, 63.6, 59.0, 51.2, 34.2, 27.6, 19.3, 17.9, 14.8. Anal. Calcd for $C_{20}H_{29}F_6N_3O_6S_2$: C, 41.02; H, 4.99; N, 7.18. Found: C, 40.93; H, 4.85; N, 7.16.

4.2.3.5. 3-(((1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyloxy)-methyl)-1-methyl-2-phenyl-4,5-dihydro-1*H*-imidazol-3-ium bis(trifluoromethylsulfonyl)amide 4e. As a white solid (75%). Mp 58.5 °C; $[\alpha]_D^{25} = -39.7$ (*c* 1.02, $CHCl_3$); MS (EI), *m/e* 328 ([M_{cation}]$^+$, 100%), 190 (27), 174 (11), 163 (33), 119 (20); MS (ESI, 0 V) *m/e* 250.1 (58%), 330.0 ([M_{cation}]$^+$, 5), 488.7 (100); IR (KBr) 3328, 3094, 3068, 2965, 2877, 2361, 1932, 1847, 1621, 1569, 1493, 1459, 1412, 1352, 1191, 1139, 1057, 935, 923, 850, 790, 774, 740, 708, 657, 619, 601, 570, 507 cm^{-1}; ^{1}H NMR (400 MHz) δ 7.74–7.49 (m, 5H), 4.60 (d, *J* = 10.4 Hz, 1H), 4.55 (d, *J* = 10.4 Hz, 1H), 4.16 (s, 4H), 3.01 (s, 3H), 3.01–2.92 (m, 1H), 2.08–1.92 (m, 1H), 1.67–1.49 (m, 3H), 1.26–1.08 (m, 2H), 0.94–0.86 (m, 1H), 0.84 (d, *J* = 7.0 Hz, 3H), 0.79 (d, *J* = 6.5 Hz, 3H), 0.77–0.64 (m, 2H), 0.63 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz) δ 166.9, 133.5, 129.8, 128.6, 120.9, 119.9 (q, J_{CF} = 321 Hz), 77.5, 74.8, 50.8, 47.9, 46.9, 39.8, 34.7, 34.1, 31.2, 25.4, 22.9, 22.0, 20.9, 15.8. HRMS (ESI): calcd for $C_{21}H_{33}N_2O$ [M^+_{cation}]: 329.2593, found 329.2597.

4.2.3.6. 3-(((1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyloxy)-methyl)-1-methyl-2-*o*-tolyl-4,5-dihydro-1*H*-imidazol-3-ium bis(trifluoromethylsulfonyl)amide (mixture of diastereomers, dr ~ 1:1.2) 4f. As a colorless liquid (69%). MS (EI), *m/e* 343 ([M_{cation}]$^+$, 100%), 329 (2), 203 (39), 175 (54); MS (ESI, 0 V) *m/e* 343.0 ([M_{cation}]$^+$, 97%); IR (NaCl) 3324, 3066, 2957, 2929, 2873, 2725, 2597, 2378, 2191, 1929, 1846, 1798, 1620, 1604, 1558, 1490, 1457, 1354, 1294, 1183, 1138, 1058, 935, 844, 788, 766, 740, 655, 617, 571, 513 cm^{-1}; ^{1}H NMR (400 MHz) (diastereomer 1, 45.5%) δ 7.60–7.44 (m, 1H), 7.46–7.31 (m, 3H), 4.60–4.36 (m, 2H), 4.31–4.07 (m, 4H), 3.03–2.84 (m, 4H), 2.26 (d, *J* = 2.3, 3H), 2.04–1.78 (m, 1H), 1.64–1.44 (m, 3H), 1.27–1.03 (m, 2H), 0.94–0.82 (m, 1H), 0.81–0.72 (m, 7H), 0.71–0.62 (m, 1H), 0.53 (d, *J* = 3.4 Hz, 3H); ^{13}C NMR (100 MHz) (diastereomer 1, 45.5%) δ 167.0, 136.7, 133.0, 131.4, 128.4, 127.2, 120.5, 119.9 (q, J_{CF} = 321 Hz), 77.3, 74.5, 50.4, 47.9, 31.3, 25.2, 22.8, 21.9, 20.8, 18.8, 15.6; ^{1}H NMR (400 MHz) (diastereomer 2, 54.5%) δ 7.60–7.44 (m, 1H), 7.46–7.31 (m, 3H), 4.60–4.36 (m, 2H), 4.31–4.07 (m, 4H), 3.03–2.84 (m, 4H), 2.26 (d, *J* = 2.3, 3H), 2.04–1.78 (m, 1H), 1.64–1.44 (m, 3H), 1.27–1.03 (m, 2H), 0.94–0.82 (m, 1H), 0.81–0.72 (m, 7H), 0.71–0.62 (m, 1H), 0.59 (d, *J* = 3.6 Hz, 3H); ^{13}C NMR (100 MHz) (diastereomer 2, 54.5%) δ 166.9, 136.9, 133.0, 131.4, 128.2, 127.1, 120.5, 119.9 (q, J_{CF} = 321 Hz), 77.4, 74.5, 50.5, 47.9, 31.1, 25.3, 22.8, 21.9, 20.8, 18.7, 15.7. Anal. Calcd for $C_{24}H_{35}F_6N_3O_5S_2$: C, 46.22; H, 5.66; N, 6.74. Found: C, 45.89; H, 5.83; N, 6.89.

4.2.3.7. (*S*)-3-Ethyl-4-isopropyl-1-methyl-2-*o*-tolyl-4,5-dihydro-1*H*-imidazol-3-ium iodide (mixture of diastereomers, dr ~ 1:1) 5. As a yellow solid (46%). MS (EI), *m/e* 245 ([M_{cation}]$^+$, 46%), 216 (8), 173 (52), 132 (5), 119 (67), 91 (26), 84 (100), 51 (51); MS (ESI, 0 V) *m/e* 245.2 ([M_{cation}]$^+$, 100%), 617.2 (2[M_{cation}]$^+$ + [M_{anion}]$^-$, 40%); IR (KBr) 3427, 2959, 2872, 1601, 1561, 1487, 1457, 1416, 1397, 1380, 1345, 1274, 1209, 1163, 1112, 1096, 1075, 1042, 947, 811, 788, 732, 595 cm^{-1}; ^{1}H NMR (400 MHz) (diastereomer 1) δ 8.19 (dd, *J* = 7.6, 1.0, 1H), 7.62–7.37 (m, 3H), 4.94–4.77 (m, 1H), 4.67 (dd, *J* = 12.8, 11.3, 1H), 3.75 (dd, *J* = 11.1, 8.7, 1H), 3.36–3.22 (m, 2H), 3.04 (s, 3H), 2.48 (s, 3H), 2.43–2.31 (m, 1H), 1.27 (t, *J* = 7.3, 3H), 1.10–1.02 (m, 6H); ^{13}C NMR (100 MHz) (diastereomer 1) δ 166.1, 135.0, 133.0, 131.9, 129.8, 127.4, 121.5, 63.2, 51.0, 40.7, 34.7, 26.9, 20.5, 18.2, 15.2, 13.0; ^{1}H NMR (400 MHz) (diastereomer 2) δ 7.62–7.37 (m, 3H), 7.23 (d, *J* = 7.7, 1H), 4.94–4.77 (m, 2H), 3.89 (dd, *J* = 10.0, 5.9, 1H), 3.36–3.22 (m, 1H), 3.16 (dq, *J* = 14.6, 7.4, 1H), 2.97 (s, 3H), 2.43–2.31 (m, 1H), 2.29 (s, 3H), 1.23 (t, *J* = 7.3, 3H), 1.10–1.02 (m, 6H); ^{13}C NMR (100 MHz) (diastereomer 2) δ 165.9, 137.0, 132.5, 130.9, 127.7, 127.6, 122.0, 63.5, 51.4, 40.1, 34.6,

27.6, 19.3, 17.9, 14.8, 13.5. HRMS (ESI): calcd for $C_{16}H_{25}N_2$ [M^+_{cation}]: 245.2018, found 245.2023.

4.2.3.8. 3-Butyl-1-methyl-2-phenyl-4,5-dihydro-1*H*-imidazol-3-ium chloride 6. As an orange, highly hygroscopic solid (65%). MS (EI), *m/e* 217 ([M_{cation}]$^+$, 100%), 77 (54), 57 (24); MS (ESI, 0 V) *m/e* 217.3 ([M_{cation}]$^+$, 100%); IR (KBr) 3412, 2960, 2933, 2873, 2427, 1607, 1574, 1491, 1462, 1446, 1375, 1299, 1077, 1029, 932, 774, 707, 657, 637, 535 cm^{-1}; ^{1}H NMR (200 MHz) δ 7.88–7.74 (m, 2H), 7.73–7.54 (m, 3H), 4.51–4.18 (m, 4H), 3.30 (t, J = 7.4 Hz, 2H), 3.05 (s, 3H), 1.73–1.50 (m, 2H), 1.25 (dq, J = 14.2, 7.2 Hz, 2H), 0.81 (t, J = 7.2 Hz, 3H); ^{13}C NMR (50 MHz) δ 165.6, 132.1, 129.1, 128.2, 121.4, 50.3, 47.7, 47.2, 34.5, 28.5, 19.0, 12.8. HRMS (ESI): calcd for $C_{14}H_{21}N_2$ [M^+_{cation}]: 217.1705, found 217.1700.

4.2.3.9. 3-Butyl-1-methyl-2-phenyl-4,5-dihydro-1*H*-imidazol-3-ium ((1*S*,4*S*)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)methanesulfonate 7. Salt **6** (29.4 mmol) was dissolved in dichloromethane (50 mL). This solution was added to (−)-camphor-10-sulfonic acid ammonium salt (29.4 mmol) in water (15 mL). The mixture was stirred for 1 h at rt. The aqueous phase was discarded. The organic phase was washed three times with a minimum amount of water. The organic phase was dried over sodium sulfate. After evaporating the solvent, ionic liquid **7** was obtained as a yellow liquid (86%). $[\alpha]_D^{25} = -19.2$ (c 1.43, $CHCl_3$); MS (EI), *m/e* 217 ([M_{cation}]$^+$, 100%), 77 (94); MS (ESI, 0 V) *m/e* 217.3 ([M_{cation}]$^+$, 100%), 665.2 (2[M_{cation}]$^+$ + [M_{anion}]$^-$, 30%); IR (KBr) 3465, 3056, 2959, 2876, 2478, 1741, 1607, 1575, 1468, 1417, 1300, 1174, 1038, 934, 855, 773, 708, 616, 582, 530 cm^{-1}; ^{1}H NMR (400 MHz) δ 7.71–7.54 (m, 5H), 4.40–4.29 (m, 2H), 4.29–4.17 (m, 2H), 3.34 (d, J = 14.7 Hz), 3.27 (t, J = 7.6 Hz, 2H), 3.01 (s, 3H), 2.88–2.76 (m, 1H), 2.81 (d, J = 14.7 Hz, 1H), 2.31 (dt, J = 18.1, 3.9 Hz, 1H), 2.08–1.92 (m, 2H), 1.86 (d, J = 18.1 Hz, 1H), 1.79–1.66 (m, 1H), 1.54 (quintuplett, J = 7.6 Hz, 2H, CH_2)), 1.42–1.29 (m, 1H), 1.26–1.16 (sextett, J = 7.6 Hz, 2H), 1.14 (s, 3H), 0.84 (s, 3H), 0.81 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz) δ 217.0, 166.3, 132.4, 129.6, 128.4, 122.3, 58.5, 50.5, 48.0, 47.7, 47.5, 46.8, 42.9, 42.5, 34.6, 29.0, 27.0, 24.4, 20.1, 19.8, 19.4, 13.4. HRMS (ESI): calcd for $C_{14}H_{21}N_2$ [M^+_{cation}]: 217.1705, found 217.1705.

4.2.4. Grignard addition to aldehydes: General procedure

Phenylmagnesiumbromide solution (2.5 mL, 1 M in THF) was placed in a Schlenk tube. The solvent was distilled off, and the remaining solid was dried under high vacuum for at least 1 h. Ionic liquid was added and the mixture was heated to 40 °C. The aldehyde was added afterwards and the mixture was stirred for 3 h. Saturated ammonium chloride solution (2.5 mL) was added and the mixture was stirred for 15 min. The mixture was extracted several times with *n*-hexane. The combined organic phases were dried over sodium sulfate. After distilling off the solvent, the raw alcohols were purified by flash column chromatography (eluent PE/EE = 20:1). *The ionic liquids were recycled as follows*: After extraction of the raw product with *n*-hexane, dichloromethane was added to the remaining mixture. The two phases were separated and the organic phase was washed five times with water. The organic phase was afterwards dried over sodium sulfate and the solvent was distilled off. The recycled ionic liquids were dried under high vacuum.

4.3.3. Grignard addition to aldehydes in the presence of Lewis acid: General procedure

Phenylmagnesiumbromide solution (2.5 mL, 1 M in THF, 3 equiv) was placed in a Schlenk tube. The solvent was distilled off, and the remaining solid was dried under high vacuum for at least 1 h. Lewis acid (0.1 equiv) and ionic liquid **4a** (6 equiv) were added and the mixture was heated to 40 °C. Hexanal (1 equiv) was added afterwards and the mixture was stirred for 3 h. Work-up was as described above.

4.3.3.1. 1-Phenylhexan-1-ol. As a slightly yellow oil. ^{1}H NMR (200 MHz) δ 7.34–7.10 (m, 5H), 4.53 (dd, J = 7.2, 6.1 Hz, 1H), 2.27 (br s, 1H), 1.81–1.46 (m, 2H), 1.32–1.10 (m, 6H), 0.78 (t, J = 6.4 Hz, 3H); ^{13}C NMR (50 MHz) δ 145.0, 128.4, 127.4, 125.9, 74.6, 39.1, 31.8, 25.5, 22.6, 14.1. The spectral data were consistent with literature values.[44]

4.3.3.2. Naphthalen-1-yl(phenyl)methanol. As a white solid. ^{1}H NMR (200 MHz) δ 8.10–7.91 (m, 1H), 7.92–7.69 (m, 2H), 7.60 (d, J = 6.7, 1H), 7.53–7.14 (m, 8H), 6.48 (s, 1H), 2.43 (s, 1H); ^{13}C NMR (50 MHz) δ 143.3, 138.9, 134.1, 130.8, 128.9, 128.7, 128.6, 127.8, 127.2, 126.3, 125.7, 125.5, 124.8, 124.1, 73.8. The spectral data were consistent with literature values.[45]

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Methylated Imidazolinium-Dithiocarboxylates: Two Representatives of a New Class of Ionic Liquids

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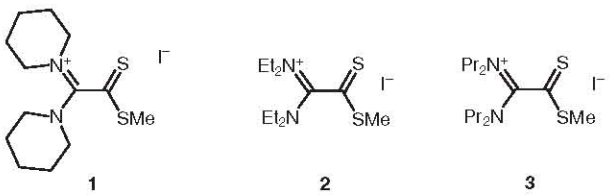
Abstract: The work describes the methylation of chiral and achiral imidazolinium-dithiocarboxylates. The resulting salts qualify as a novel class of ionic liquids after an anion metathesis was performed. Their NMR and UV/Vis spectra were studied.

Key words: ionic liquids, chirality, chiral cations, imidazolinium salts, zwitterions

Ionic liquids have emerged as a new promising class of organic material due to their potential as novel solvents for reactions and electrochemical processes.[1] Some of these liquids are expected to be 'green solvents', for example, due to their negligible vapor pressure.[2] The organic salts have a melting point below 100 °C. An additional advantage is the efficient recovery of some of these salts. Nevertheless, in a few examples it is known that the ionic liquids are not inert and react with some reagents,[3] which could be a disadvantage in some applications. The collection of ionic liquids based on the combinations of cations and anions has dramatically increased, and constantly new salts[4] and solvent mixtures[5] are prepared. In case the ionic liquids are chiral, they have an additional potential as chiral solvents, shift reagents, and catalysts.[6]

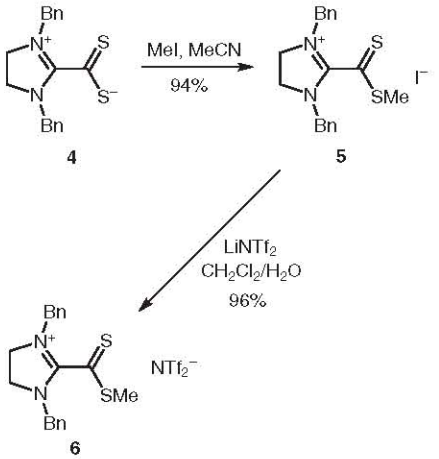
Due to our efforts in ionic liquids[7] and imidazolinium-dithiocarboxylates[8] we were interested to explore the possibility to prepare a new interesting class of ionic liquids from imidazolinium-dithiocarboxylates. The latter belong to the extraordinary class of carbene complexes of nonmetals[9] and can be formally prepared by the addition of an imidazolinium carbene to CS_2. The CS_2 group is nearly perpendicular to the imidazolinium ring. It is known that the CS_2 group can be methylated to give salts as shown in Figure 1. However, the examples in the literature are very limited and only simple salts with very high melting points were reported.[10]



1 2 3

Figure 1 Salts 1–3

First, the simple zwitterion **4**[11] was prepared according to the literature. The zwitterion was then transferred into salt **5** with methyl iodide in 94% yield. The salt, as the starting zwitterion, was red and had a melting point of 145 °C. Through an anion metathesis, NTf_2 was introduced as an anion and the resulting red salt **6** was obtained in 96% yield with a water content of 0.069% (Scheme 1). The salt is liquid at room temperature and remains a liquid even at storage in a freezer at –28 °C for several months.



4 5 6

Scheme 1

Next, an enantiopure analogue was prepared. Starting from diamine **7** the zwitterion **8** was prepared in analogy to zwitterion **4**. Treating diamine **7** with of DMF dimethylacetal at 100 °C resulted in the carbene dimer, which was directly dissolved in xylene and reacted with CS_2 at 140 °C for 45 minutes to give the desired zwitterion **8** in 43% yield.[12] Treatment of **8** with methyl iodide gave the desired salt **9** in 92% yield. The salt has a melting point of 87 °C. In addition it was possible to change the counter anion by stirring salt **9** with KPF_6 or $LiNTf_2$ in a mixture of CH_2Cl_2 and water, which gave the desired salts **10** and **11** in 88 and 98% yield, respectively (Scheme 2). Interestingly, salt **10** with a PF_6 counter anion had a melting point of 74 °C, while salt **11** with the more lipophilic NTf_2 anion had a higher melting point of 109 °C. The salts were as stable as their so far reported analogues in the literature and no decomposition was observed at their melting points.

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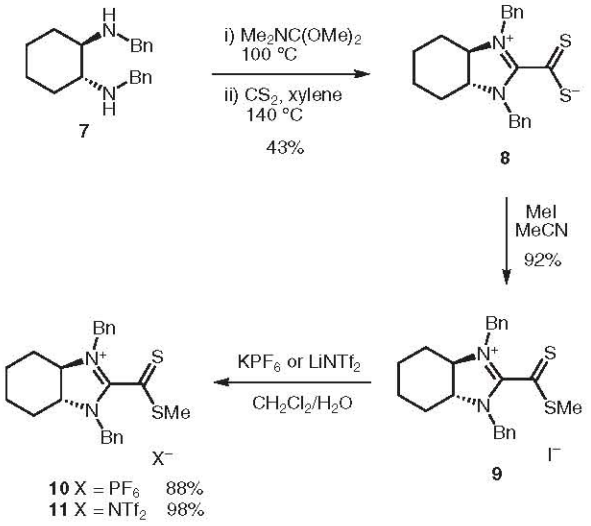

Scheme 2

The salts displayed some interesting behavior in the ^{1}H NMR spectra. While the diastereotopic benzylic protons came in salt **5** as a singlet at $\delta = 4.69$, they showed in salt **6** a typical AB system, one doublet at $\delta = 4.65$ and one at $\delta = 4.51$. Although achiral, it is obvious that through desymmetrization a new chiral center would be formed at the benzylic position and the salt would possess an axial chirality along the axis of the imidazolinium ring and the CS_2Me group. In addition it was possible to observe in salts **9**, **10**, and **11** only very broad singlets for the benzylic protons, which is due to the slow rotation of the CS_2Me group at room temperature. However, this rotation is suppressed at 0 °C. A ^{1}H NMR spectrum at this temperature showed for salt **10** the first AB system with two doublets at $\delta = 5.00$ and 4.88 and the second AB system with two doublets at $\delta = 4.84$ and 4.70.

Because of the red color of the cation, due to charge transfer, it is also possible to observe different shifts in the UV/Vis spectra depending on the lipophilicity of the counter anions. In chloroform, salt **9** had a maximum at $\lambda = 422$ nm, salt **10** at 498 nm, and salt **11** at 504 nm. Changing the solvent to methanol, salt **9** had a maximum at $\lambda = 500$ nm.

In conclusion, we have demonstrated that methylated imidazolinium salts qualify as new chiral and room temperature ionic liquids. Because of their straightforward synthesis, it will be possible to prepare various analogues and to incorporate an axial chirality. Use of other alkylation agent instead of methyl iodide is also possible.[13] Due to their color it is possible to use these salts to determine the polarity of solvents and the lipophilic character of anions.[14]

All reactions were conducted under a protective atmosphere of dry N_2. MeCN and CH_2Cl_2 were distilled from CaH_2. Anhyd xylene was purchased from Sigma-Aldrich and used without further purification. Reactions were monitored by TLC with Merck silica gel 60 F_{254} plates. Flash column chromatography was performed on silica gel 60 (70–230 mesh ASTM). IR spectra were recorded on a Vector 22 FT-IR spectrophotometer from Bruker. ^{1}H NMR spectra were taken on an AMX 400 (400 MHz) or on an AC 250 P (200 MHz) spectrometer from Bruker in $CDCl_3$ and calibrated using the peak at 7.26 ppm as an internal reference. ^{13}C NMR spectra were taken on an AMX 400 (100 MHz) or on an AC 250 P (50 MHz) spectrometer from Bruker in $CDCl_3$ and calibrated using the peak 77.2 ppm as an internal reference. Mass spectra were recorded on MS 5889 B mass spectrometer from Hewlett Packard. Electron spray mass spectrometry was performed directly on a MS LC/MSD 1100 MSD mass spectrometer from Hewlett Packard. Elemental analysis were carried out on a 'Elementar Analyzer', model 1106 from Carlo Erba Instrumentazione at the Institute of Pharmaceutical Chemistry of the Technical University of Braunschweig and are reported as the average of two runs. Optical rotations were measured using a 1 dm path length (*c* is given as g/100 mL) on a PerkinElmer 243 B polarimeter in the reported solvent. UV/Vis spectra were recorded on a Hewlett Packard 8452A Diode Array Spectrophotometer. Melting points were taken on a Dr. Tottoli apparatus from Büchi and are uncorrected. H_2O content was determined via the Karl Fischer method. 1,3-Dibenzylimidazolinium-2-dithiocarboxylate (**4**)[11] and (1*R*,2*R*)-*N*,*N*-dibenzylcyclohexane-1,2-diamine (**7**)[15]were prepared according to the literature. All other chemicals were purchased from Aldrich, Fluka, Merck, or Lancaster.

1,3-Dibenzyl-2-(methylthiocarbonothioyl)imidazolinium Iodide (5)

MeI (0.5 mL, 8 mmol) was added to 1,3-dibenzylimidazolinium-2-dithiocarboxylate (**4**; 200 mg, 0.673 mmol) in MeCN (4 mL) to give, after 16 h, a deep red solution. The solvent was removed and the crude product obtained was washed with Et_2O (10 mL) to give the expected product as a red solid (269 mg, 0.63 mmol, 94%); mp 145 °C.

IR (KBr): 3424, 2897, 1612, 1264, 1122, 1059, 740 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.45$–7.31 (m, 10 H, C_6H_5), 4.68 (s, 4 H, NCH_2Ph), 4.52–4.43 (m, 2 H, NCH_2CH_2N), 3.74–3.59 (m, 2 H, NCH_2CH_2N), 2.93 (s, 3 H, CH_3).

^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 208.0$ (CS_2), 164.4 (CN_2), 131.7 (C_6H_5), 129.4 (C_6H_5), 129.3 (C_6H_5), 128.6 (C_6H_5), 52.0 (NCH_2Ph), 48.4 (NCH_2CH_2N), 20.6 (CH_3).

MS (ESI, 0 V): *m*/*z* = 341 (M^+, 100%).

Anal. Calcd for $C_{19}H_{21}IN_2S_2$: C, 48.72; H, 4.52; N, 5.98. Found: C, 48.52; H, 4.57; N, 6.31.

1,3-Dibenzyl-2-(methylthiocarbonothioyl)imidazolinium Bis(trifluoromethylsulfonyl)amide (6)

An anion metathesis was performed with **5** (100 mg, 0.213 mmol) in CH_2Cl_2 (5 mL) with a solution of $LiNTf_2$ (92 mg, 0.319 mmol) in H_2O (5 mL). After stirring vigorously for 30 min, the organic phase was washed with H_2O (3 × 5 mL) and dried (MS 3 Å) to give the desired product as a red liquid (127 mg, 0.21 mmol, 96%).

IR (NaCl): 1599, 1350, 1190, 1133, 1054 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.44$–7.36 (m, 6 H, C_6H_5), 7.31–7.26 (m, 4 H, C_6H_5), 4.65 (d, $J = 14.0$ Hz, 2 H, NCH_2Ph), 4.51 (d, $J = 14.0$ Hz, 2 H, NCH_2Ph), 4.21–4.01 (m, 2 H, NCH_2CH_2N), 3.71–3.62 (m, 2 H, NCH_2CH_2N), 2.96 (s, 3 H, CH_3).

^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 207.6$ (CS_2), 163.5 (CN_2), 131.4 (C_6H_5), 129.6 (C_6H_5), 129.5 (C_6H_5), 128.6 (C_6H_5), 120.1 (q, $J = 319.0$ Hz, CF_3), 51.6 (NCH_2Ph), 47.7 (NCH_2CH_2N), 20.3 (CH_3).

MS (ESI, 0 V): *m*/*z* = 341 (M^+, 100%).

Anal. Calcd for $C_{21}H_{21}F_6N_3O_4S_4$: C, 40.57; H, 3.40; N, 6.76. Found: C, 40.93; H, 3.44; N, 6.81.

(3*R*,7*R*)-1,3-Dibenzyl-3,4,5,6,7,7-hexahydrobenzoimidazol-1-ium-2-dithiocarboxylate (8)

(1*R*,2*R*)-*N*,*N*-Dibenzylcyclohexane-1,2-diamine (**7**; 3 g, 10.2 mmol) was heated in the presence of DMF dimethylacetal (8.5 mL, 61.1 mmol) at 100 °C in a distillation set in order to remove MeOH and Me_2NH formed during the reaction. After 2 d, the temperature was raised to 115 °C and after slow evaporation, the mixture was dried overnight under vacuum at r.t. Thereafter, xylene (7.5 mL) and CS_2 (6 mL, 99.3 mmol) were added. After 45 min heating at 140 °C, the mixture was evaporated and the red solid was washed with hexane (20 mL) (1.45 g, 3.82 mmol, 38%); mp 209 °C; $[\alpha]_D^{22}$ +288 (*c* = 1.09, $CHCl_3$).

IR (KBr): 3423, 2945, 1521, 1454, 1365, 1261, 1065, 1047, 755, 713, 696 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.55–7.52 (m, 4 H, C_6H_5), 7.42–7.33 (m, 6 H, C_6H_5), 4.82 (d, *J* = 15.5 Hz, 2 H, NCH_2Ph), 4.65 (d, *J* = 15.5 Hz, 2 H, NCH_2Ph), 3.29–3.18 (m, 2 H, 2 NCH), 1.94–1.73 (m, 4 H, 2 $NCHCH_2$), 1.32–1.11 (m, 4 H, 2 $NCHCH_2CH_2$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 225.9 (CS_2), 169.9 (CN_2), 134.0 (C_6H_5), 128.9 (C_6H_5), 128.5 (C_6H_5), 66.9 (NCH_2Ph), 50.2 (NCH), 28.3 ($NCHCH_2$), 23.9 ($NCHCH_2CH_2$).

MS (EI): *m*/*z* (%) = 379 (M^+, 18), 289 (34), 106 (33), 91 (100).

Anal. Calcd for $C_{22}H_{24}N_2S_2$: C, 69.43; H, 6.36; N, 7.36. Found: C, 69.06; H, 6.39; N, 7.56.

(3*R*,7*R*)-1,3-Dibenzyl-2-(methylthiocarbonothioyl)-3,4,5,6,7,7-hexahydrobenzoimidazol-1-ium Iodide (9)

MeI (0.5 mL, 8 mmol) was added to **8** (200 mg, 0.525 mmol) in MeCN (4 mL) to give after 16 h, a very deep red solution. The solvent was removed and the obtained crude product was washed with Et_2O (10 mL) to give the expected product as a red solid (252 mg, 0.483 mmol, 92%); mp 87 °C; $[\alpha]_D^{22}$ –103 (*c* = 1.06, $CHCl_3$).

IR (KBr): 3423, 2938, 2859, 1547, 1453, 1264, 1098, 1030, 695 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.47–7.39 (m, 10 H, C_6H_5), 4.83 (br s, 5 H, NCH_2Ph, NCH), 3.55 (br s, 1 H, NCH), 2.86 (s, 3 H, SCH_3), 1.96–1.64 (m, 4 H, 2 $NCHCH_2CH_2$), 1.40–1.05 (m, 4 H, $NCHCH_2CH_2$).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 208.7 (CS_2), 167.2 (CN_2), 130.7 (C_6H_5), 129.2 (C_6H_5), 128.9 (C_6H_5), 127.8 (C_6H_5), 68.7 (NCH_2Ph), 51.0 (NCH), 28.7 ($NCHCH_2CH_2$), 27.3 ($NCHCH_2CH_2$), 23.8 ($NCHCH_2CH_2$), 20.8 (SCH_3).

MS (ESI, 0 V): *m*/*z* = 395 (M^+, 100%).

Anal. Calcd for $C_{23}H_{27}N_2S_2$: C, 52.87; H, 5.21; N, 5.36. Found: C, 52.33; H, 5.23; N, 4.95.

(3*R*,7*R*)-1,3-Dibenzyl-2-(methylthiocarbonothioyl)-3,4,5,6,7,7-hexahydrobenzoimidazol-1-ium Hexafluorophosphate (10)

An anion metathesis was carried out on **9** (274 mg, 0.525 mmol) in CH_2Cl_2 (5 mL) with a solution of KPF_6 (126 mg, 0.68 mmol) in H_2O (5 mL). After stirring vigorously for 30 min, the organic phase was washed with H_2O (3 × 5 mL) and dried (MS 3 Å) to give the desired product as a red solid (251 mg, 0.46 mmol, 88%); mp 74 °C; $[\alpha]_D^{22}$ +62 (*c* = 1.05, $CHCl_3$).

IR (KBr): 3431, 2945, 1550, 1455, 1267, 838 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.41–7.29 (m, 10 H, C_6H_5), 4.71 (br s, 4 H, NCH_2Ph), 4.24 (br s, 1 H, NCH), 3.45 (br s, 1 H, NCH), 2.87 (s, 3 H, SCH_3), 1.93–1.67 (m, 4 H, 2 $NCHCH_2CH_2$), 1.32–1.04 (m, 4 H, $NCHCH_2CH_2$).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 208.3 (CS_2), 166.7 (CN_2), 132.1 (C_6H_5), 129.3 (C_6H_5), 129.0 (C_6H_5), 127.7 (C_6H_5), 68.4 (NCH_2Ph), 50.4 (NCH), 28.6 ($NCHCH_2CH_2$), 27.5 ($NCHCH_2CH_2$), 23.7 ($NCHCH_2CH_2$), 20.2 (SCH_3).

MS (ESI, 0 V): *m*/*z* = 395 (M^+, 100%).

Anal. Calcd for $C_{23}H_{27}F_6N_2PS_2$: C, 51.10; H, 5.03; N, 5.18. Found: C, 51.21; H, 5.35; N, 5.11.

(3*R*,7*R*)-1,3-Dibenzyl-2-(methylthiocarbonothioyl)-3,4,5,6,7,7-hexahydrobenzoimidazol-1-ium Bis(trifluoromethylsulfonyl)amide (11)

An anion metathesis was performed with **9** (100 mg, 0.191 mmol) in CH_2Cl_2 (5 mL) with a solution of $LiNTf_2$ (113 mg, 0.393 mmol) in H_2O (5 mL). After stirring vigorously for 30 min, the organic phase was washed with H_2O (3 × 5 mL) and dried (MS 3 Å) to give the desired product as a red solid (126 mg, 0.187 mmol, 98%); mp 109 °C; $[\alpha]_D^{22}$ +50 (*c* = 1.185, $CHCl_3$).

IR (KBr): 3441, 2950, 1556, 1348, 1191, 1134, 1057 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.41–7.29 (m, 10 H, C_6H_5), 4.67 (br s, 4 H, NCH_2Ph), 4.09 (br s, 1 H, NCH), 3.48 (br s, 1 H, NCH), 2.88 (s, 3 H, SCH_3), 1.97–1.61 (m, 4 H, 2 $NCHCH_2CH_2$), 1.35–1.05 (m, 4 H, $NCHCH_2CH_2$).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 208.1 (CS_2), 166.8 (CN_2), 132.2 (C_6H_5), 129.3 (C_6H_5), 129.1 (C_6H_5), 127.7 (C_6H_5), 120.2 (q, *J* = 319 Hz, CF_3), 68.6 (NCH_2Ph), 50.5 (NCH), 28.5 ($NCHCH_2CH_2$), 27.7 ($NCHCH_2CH_2$), 23.6 ($NCHCH_2CH_2$), 20.2 (SCH_3).

MS (ESI, 0 V): *m*/*z* = 395 (M^+, 100%).

Anal. Calcd for $C_{25}H_{27}F_6N_3O_4S_4$: C, 44.43; H, 4.03; N, 6.22. Found: C, 44.59; H, 4.19; N, 6.40.

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An easy way to produce α-iron filled multiwalled carbon nanotubes

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Abstract

α-Iron filled multiwalled carbon nanotubes were prepared through filling of commercially available carbon nanotubes, after oxidative opening, with ferrofluid particles. After washing and reduction with hydrogen clean tubes filled with α-iron were obtained.

1. Introduction

The research field of carbon nanotubes [1,2] (CNTs) has received a continuous growing interest since these tubes were discovered in 1991 [3]. Many efforts have been made to fill single- and multiwalled carbon nanotubes with different materials [4–6]. Especially carbon nanotubes, filled with metals, can be used for various applications in nanotechnology [7–11], biomedical sciences [12] and memory device technology [13]. Moreover, they also have a potential as catalyst in various reactions [14]. Several procedures have been developed in order to fill carbon nanotubes via capillary action [15,16] or wet chemical method [17]. In addition, it is possible to prepare in situ filled carbon nanotubes e.g. with an arc discharge technique [18], through chemical vapor deposition techniques [19] or via pyrolysis of organometallic compounds [20,21]. However, often with these methods the level of filling is not satisfying. A method to obtain a relatively dense packing of 50 nm diameter solid particles in large 500 nm diameter MWCNTs was reported by the group of Bau [22]. Since we desired in our group multiwalled carbon nanotubes filled with ferromagnetic or paramagnetic material, we became interested in the work of the group of Gogotsi [23]. In their work, they could show impressively that it was possible to fill carbon nanotubes with a diameter of 300 nm, prepared in their CVD process using alumina membrane as templates, to a high degree with commercially available ferrofluid. We were interested to extend this procedure to commercially available carbon nanotubes, prepared from an arc-discharge procedure. Due to smaller diameter of the tubes and a higher degree of graphene structural perfection in the tube walls, this would be beneficial in possible applications. More important, we were interested to transform the magnetite particles of the ferrofluid into α-iron, which could be advantageous in magnetic applications. In the present work, we provide an easy and generalized route to prepare α-iron filled multiwalled carbon nanotubes.

2. Experimental

With the goal of obtaining a high filling ratio in carbon nanotubes, we explored a simple method based on solution phase chemistry for high yield (>70%) filling of multiwalled carbon nanotubes with Fe_3O_4 nanoparticles. As a source we used commercially available organic based ferrofluid (EMG 911) (Ferrotec Corporation) for the filling of purified MWNT. These ferrofluids carry magnetite (Fe_3O_4) particles with a characteristic diameter which ranges from 8 to 18 nm. MWCNTs used for our experiments were purchased from SES Research (TX, USA) (formed by arc discharge, with a diameter ranges from 2 to 20 nm) and Sun Nano (China) (formed by CVD process, with a diameter ranges from 20 to 70 nm).

The microstructures of the samples obtained were observed with TEM on Philips CM200 FEG (operated at 120 kV) and Philips CM 400 (operated at 200 kV) transmission electron microscope equipped with an energy-dispersive X-ray spectrometer (EDS). Samples for TEM were

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prepared by dispersing the nanotubes in 2-propanol and then placing them onto a copper grid coated with holey carbon film. The XRD pattern of the composites were collected on ISO-Debyeflex 2002 Model III diffractometer operated at 35 kV and 35 mA with a copper tube.

For the filling experiments purified and opened nanotubes bought from SES Research were used as received and nanotubes bought from Sun Nano were purified using potassium permanganate in acidic solution by the method described by Hiura et al. [24]. MWCNTs treated with potassium permanganate solution in H_2SO_4 were filtered on a porous glass filter (P-16) Schott Duran and washed with water to neutral pH. It was then further washed with ethanol and then dried in an oven at 60 °C for overnight.

The samples so obtained were kept in a round bottomed flask, made wet by a few drops of organic based ferrofluid EMG-911 (Ferrotec) and kept overnight for filling. Samples were then washed thoroughly with acetone and further with xylene, dried in an oven at 60 °C overnight. The dried samples were then reduced under a stream of H_2/Ar (100/500 ccm) at 645 °C for 20 h. Water based ferrofluid EMG-508 (Ferrotec) was also used for filling.

3. Results and discussion

Fig. 1 shows two TEM images of the filled MWCNTs prior to washing. Next to the high extent of particles inside the tubes, it is also noticeable that many particles are attached outside on the tube walls. Fig. 2 shows the TEM images of purified filled nanotubes before reduction and Fig. 3 depicts high resolution TEM images of nanotubes after the reduction. From these images it is possible to see that the nanotubes are filled with a large amount of ferromagnetic particles. It was possible to observe that the tubes with an inner diameter close to 10 nm or less than 10 nm were less filled or remained empty. This was expected as the average size of the particles in the ferrofluid was 10 nm. It could also be possible that a few tubes were

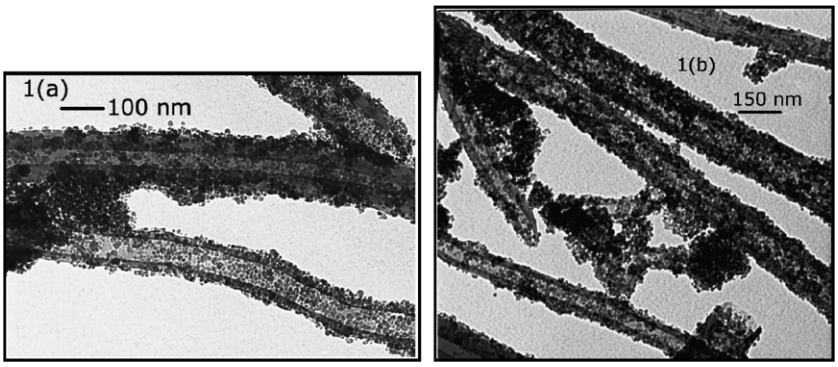

Fig. 1. (a, b) Low resolution TEM images of filled MWCNTs prior to washing.

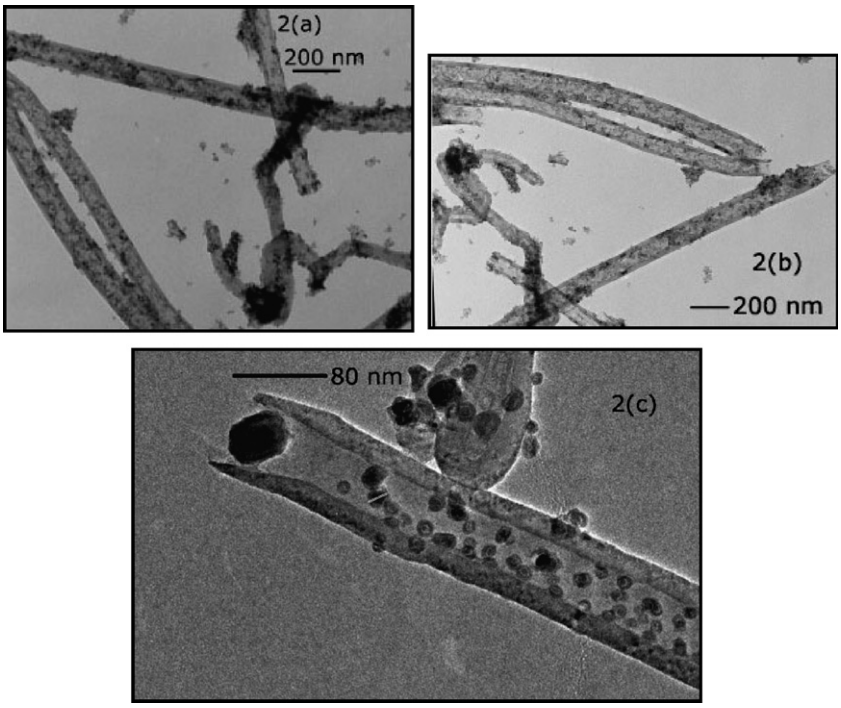

Fig. 2. (a–c) TEM images of purified filled nanotubes.

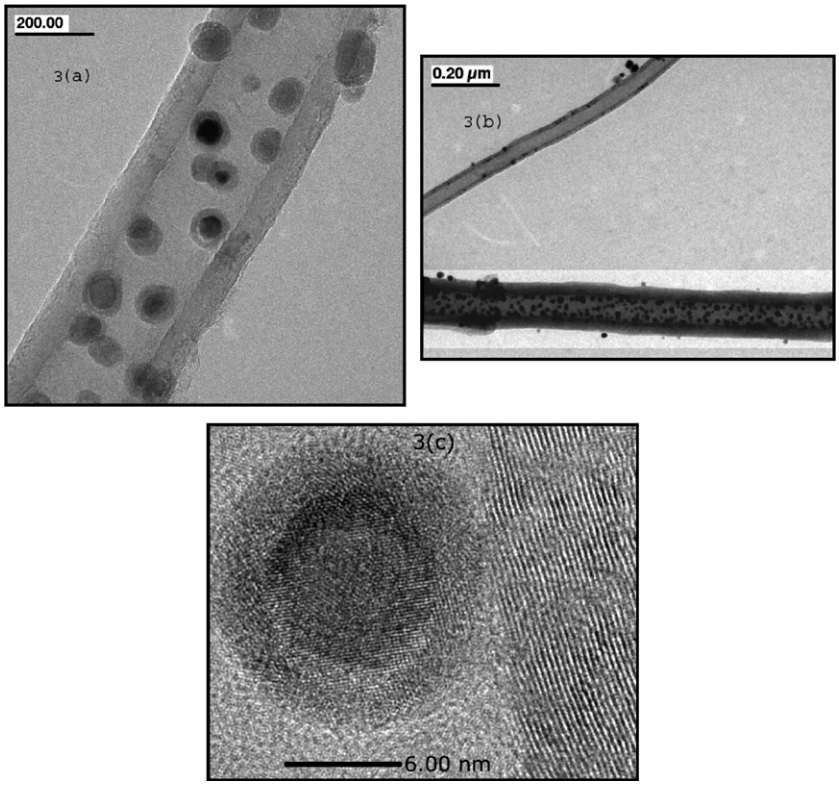

Fig. 3. (a, b) TEM images of filled nanotubes reduced at 645 °C; (c) HRTEM image of a particle inside the tube adjacent to the tube wall.

not filled due to insufficient opening. Tubes with a higher diameter of 20–25 nm were filled almost completely. Up to 80% of a tube's inner space was filled with a large amount of Fe nanoparticles, which satisfied our goal to obtain ferromagnetic nanotubes. In the filled parts particles filled out up to 50% of the inner volume of tubes. The fringes, visible in a high resolution image, of a particle inside the tube (Fig. 3c) revealed its crystalline nature.

In a further experiment sequential images were taken with a double tilt holder randomly at different angles, which proved that the particles were indeed inside the tubes (see Fig. 4). When the experiment was performed with water based ferrofluid EMG-508 (Ferrotec) a much lower level of filling was observed.

Fig. 5 represents the EDS measurement of the filled carbon nanotubes, which confirmed the presence of atomic iron in the MWCNTs. The thin coating around the Fe particles as shown in Fig. 3c is expected to be of carbon, which might result from the pyrolysis of the surfactant during reduction at 645 °C. The surfactant covering Fe_3O_4

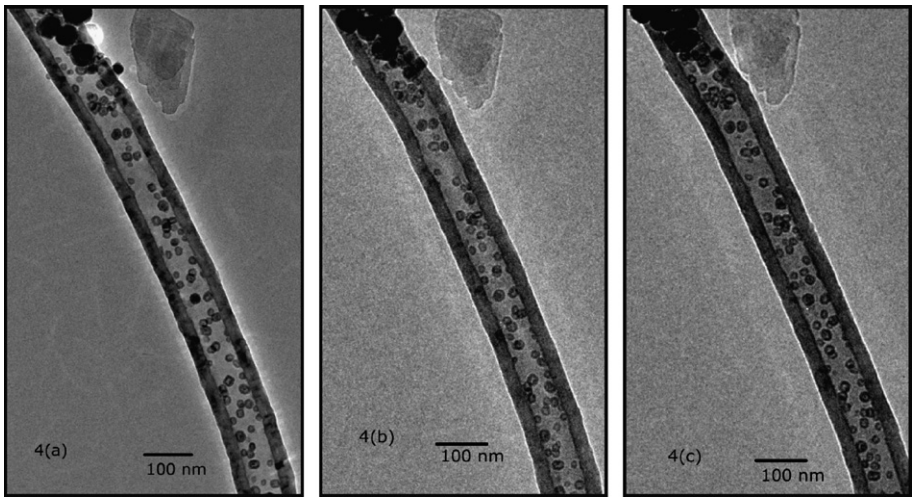

Fig. 4. TEM images taken sequentially at tilt angles (a) 0°; (b) 5°; (c) 10° showing the particles sticking on the wall (see on the top of the image) and particles inside the tube.

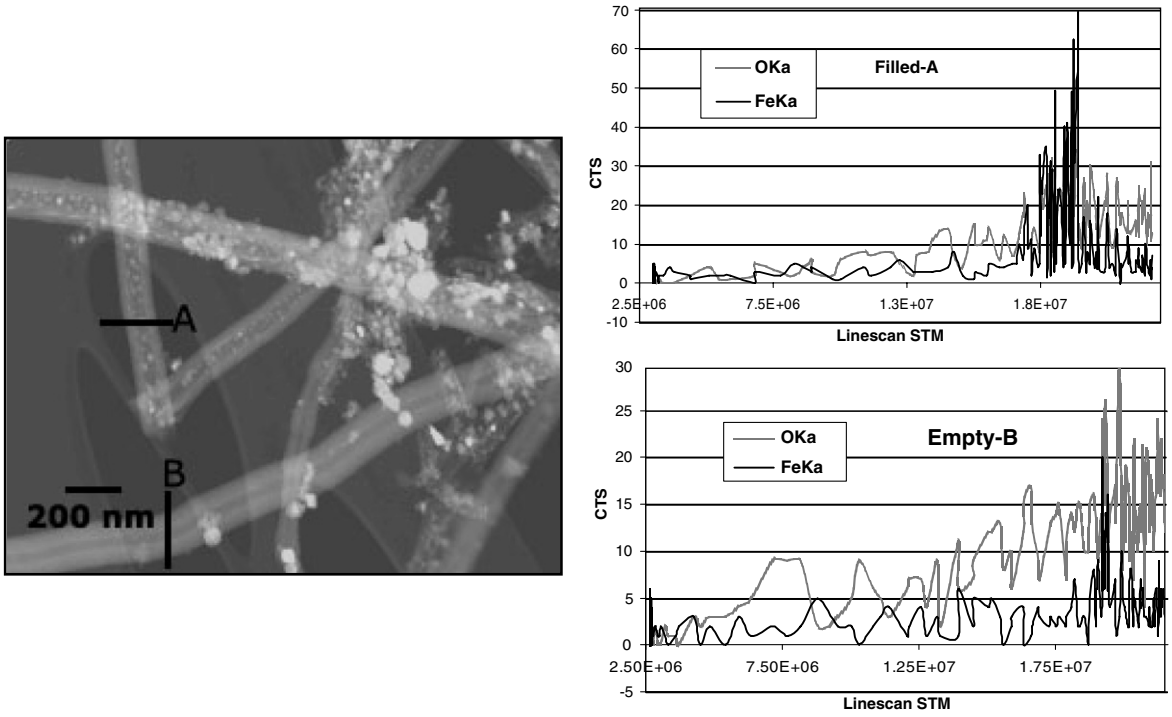

Fig. 5. Line scan EDX spectra of empty and filled tubes. It can be seen that at the empty part O percentage is much higher (Plot-B) than Fe as compared to the ratio of Fe/O in filled part of the tube (Plot-A).

nanoparticles is used to stabilize them and make them soluble in organic solvents. Since some Oxygen was observed in the bulk EDX spectra which suspected the presence of FeO, a line scan across a well filled part and another across a not filled part were made. It was found that in the second spectra Oxygen count was higher than Fe, while in the spectra taken across a well filled portion the Fe count was much higher than Oxygen. This should eliminate the possibility of oxygen present as FeO.

Fig. 6 shows the corresponding selected area electron diffraction patterns taken from the filled nanotube shown in Fig. 3b. The diffraction pattern shows sharp and clear spots indicating that the particles inside the nanotubes are composed of single crystals.

Fig. 7 represents XRD patterns of the samples shown in Figs. 2 and 3 (filled and after annealing at 645 °C under hydrogen). Pattern of the filled sample (1) and sample (2)

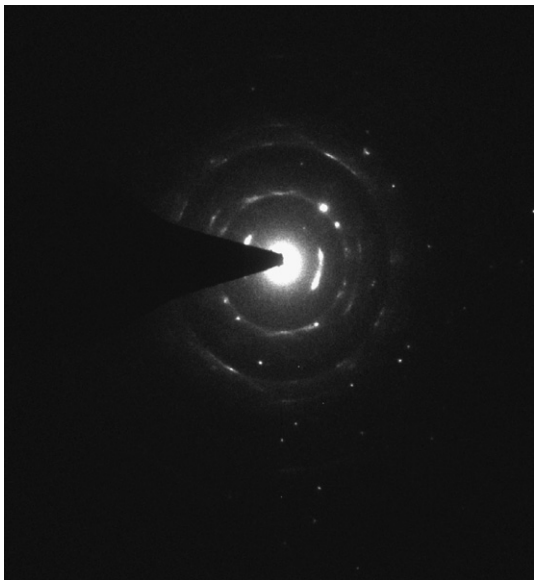

Fig. 6. Selected area electron diffraction pattern of an Iron filled nanotube. The two arcs close to central spot result from the 002 scattered beams emitted by the tube walls, corresponding to the regular intergraphene distance at 0.34 nm.

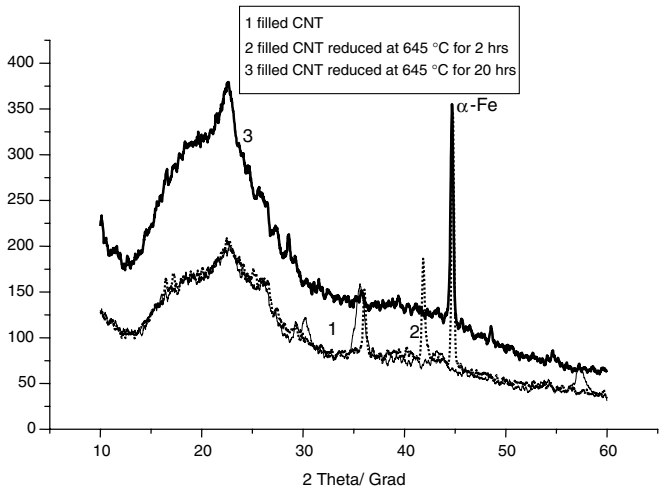

Fig. 7. XRD pattern of filled (1) samples and samples after annealing for 2 h (2) and 20 h (3).

(reduced at 645 °C for 2 h) revealed the presence of a small amount of α-Fe and various phases of iron in the filled tubes. After the annealing process all different phases of iron were completely transformed into α-Fe. In our experiments, we observed as depicted in graph 2 and 3, that for a complete conversion to α-Fe a longer annealing time was necessary.

4. Conclusion

In summary, a simple wet chemical route was developed to fill commercially available multiwalled carbon nanotubes with magnetic Fe_3O_4 particles. Further reduction of the filled MWCNTs resulted in tubes filled with α-iron. These α-iron-filled MWCNTs may have potential applications in chemistry as catalyst support. Also they might be found useful for drug delivery and other biomedical applications.

Acknowledgements

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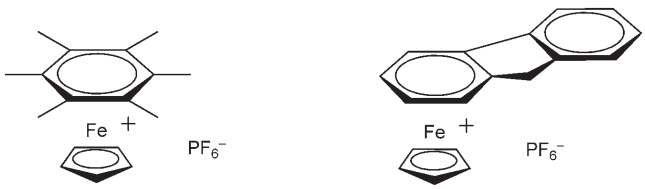
Carbon nanocapsules

DOI: 10.1002/smll.200600004

Solid-State Synthesis of Well-Defined Carbon Nanocapsules from Organometallic Precursors**

*Dheeraj Jain, Andreas Winkel, and René Wilhelm**

After the discovery of carbon nanotubes in 1991 by Iijima,[1] various structures, which are more or less related to fullerenes, including single-wall and multiwalled carbon nanotubes,[1–3] carbon nanohorns,[4–6] carbon nanospheres,[7–10] and onion-like carbon structures[11,12] have been prepared. Such structures, if containing metals,[13–15] have additional potential as magnetic particles, contrast agents, protecting cloaks, catalysts, and in other applications. In spite of their emerging applications, such metal-filled structures are relatively difficult to produce in bulk quantities when compared to pure carbon nanotubes and have sometimes been produced merely as by-products during the preparation of carbon nanotubes.[9,16,17] Several of the procedures involve arc-discharge using metal-doped graphite rods,[5,18] the pyrolysis of non-graphitizing carbon material,[19,20] or catalytically assisted chemical vapor deposition (CCVD).[21,22] Most of these procedures require relatively complex setups and have limitations over the range of metals and the amount of filling. Here we describe a straightforward method by which novel nanocarbon structures, namely, carbon nanocapsules filled with an Fe–P composite, can be obtained. The new particles are obtained via the simple pyrolysis of the [CpFe(arene)] salt **1** (see Scheme 1). It is well known that the pyrolysis of different organometallic complexes in a sealed vessel can lead to carbon nanotubes,[23,24] nanocables,[25] and onions.[26] In addition, the pyrolyis of ferrocene in an open system with a flow of argon with or without a hydrocarbon source leads to carbon nanotubes.[27–30] However, the structures in the presented work have not been reported so far and can be obtained in near-quantitative yield from complex **1**.



1 2

Scheme 1. Ferrocenyl complexes **1** and **2** used in this study.

Complex **1**[31] was pyrolyzed at 700 °C for 2 h in a sealed quartz tube in order to give carbon nanocapsules in near quantitative yield. Prior to TEM measurements, the samples were washed with concentrated HCl in order to remove iron and other impurities. When complex **2**[32] (see Scheme 1) was pyrolyzed at 700 °C, rather deformed, undefined, and unfilled tubular structures were formed. This result showed that the structures produced are highly dependent on the starting complex used in the pyrolysis reaction.

Representative images of the morphology of the obtained samples are shown in Figure 1. The low-resolution images (Figure 1a and b) reveal that the samples contained a large quantity of capsules with an average diameter of 100 nm, an average wall thickness of 16 nm, and a length varying from 220 to 700 nm with no other amorphous carbon by-products. This result suggests that a near-quantitative yield of the nanocapsules is obtained. High-magnification HRTEM images of such capsules are shown in Figure 2a, while Figure 2b and c displays a few capsule-like structures, which were either poorly developed (Figure 2b) or deformed (Figure 2c).

The capsules consist of a thick wall of carbon and are filled with a noncrystalline composite material containing mainly Fe and P, which could be characterized by using energy-dispersive spectroscopy (EDS). Since the walls were not graphitized, as is the case with multiwalled carbon nanotubes, one of the obtained sample was heated under argon at 700 °C for 12 h. The resulting material was analyzed; the results are depicted in Figure 3. The procedure had no influence on the wall structure, however, the amorphous Fe–P composite was transformed into a crystalline structure. Figure 3a represents a high-magnification HRTEM image of such a capsule showing the wall structure and the material inside the capsule. Figure 3b shows the selected-area electron diffraction (SAED) pattern taken from such a filled capsule.

To analyze the chemical composition of the filling material, we also performed EDS measurements. Figure 4 shows the EDS image of the filled capsules, which confirmed the presence of Fe and P within the capsules. The detected Cu is due to the TEM grid. The diffraction pattern shown in Figure 3b and the presented EDS pattern confirms that the nanoparticles within the capsules are composed of a crystalline Fe–P composite when heated under argon at 700 °C for 12 h.

The experiments were also performed at higher temperature and for different time intervals while keeping other parameters constant. It was found that 700 °C was the most suitable temperature for obtaining such nanocapsules. When the reaction temperature was increased, the presence of amorphous carbon was observed in the product to a greater

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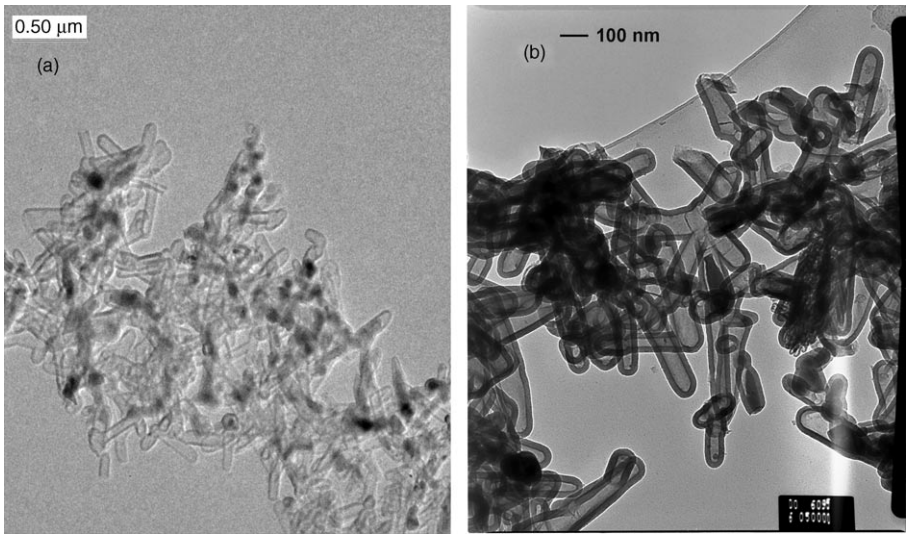

Figure 1. a) A typical TEM image of the produced nanocapsules; b) another TEM image taken at higher magnification.

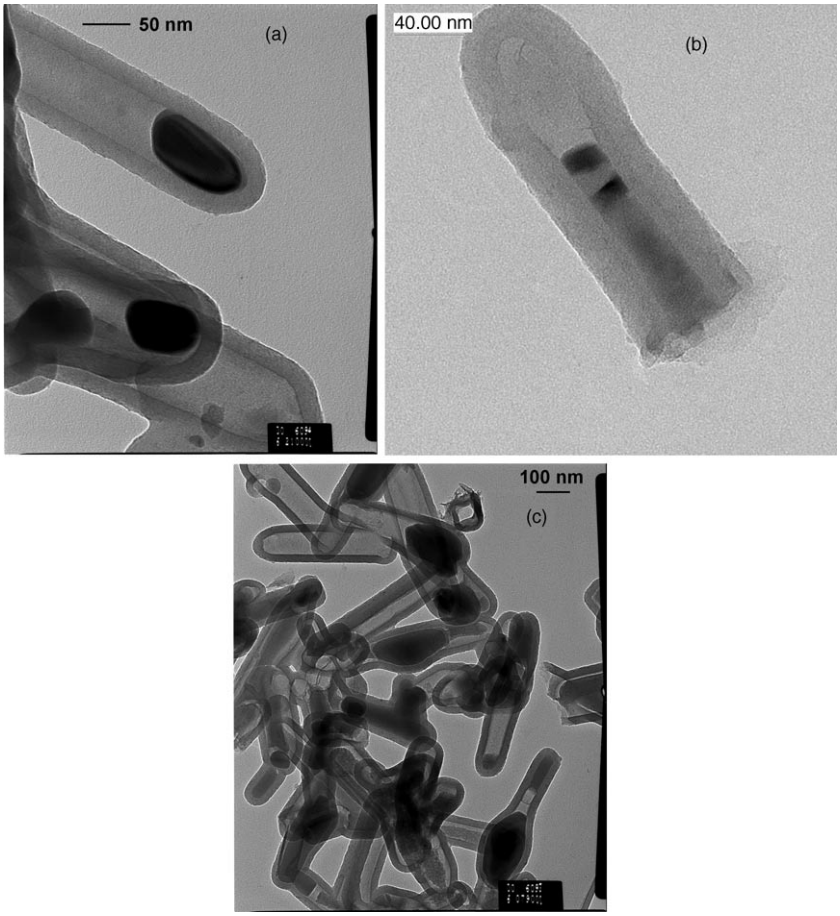

Figure 2. HRTEM images of a) nanocapsules showing the wall structure and amorphous material contained inside the capsule walls; b) a poorly developed capsule. c) A HRTEM image showing that a few of the capsules were deformed.

extent. At 900 °C, longer and less well-defined tubular structures were formed.

The results of these experiments are very different to those that were obtained from other systems where the pyrolysis of organometallic compounds in a sealed system has been reported.[23–26] In those cases, carbon nanotubes have mainly been observed as the resulting product. In the present case, the pyrolysis of complex **1** resulted in the observed nanocapsules, which may be also classified as very short carbon fibers, due to the lack of well-graphitized walls, such as those that are found in carbon nanotubes. Establishing a reason for the outcome of these experiments is difficult, since results in the solid-state synthesis can differ when slightly different analogues of the precursor complex are applied. In the present case, the application of a hexafluorophosphate salt may be an explanation.

In summary, it has been shown that the [CpFe(arene)] derivative **1** yielded unique carbon structures in near quantitative yield upon pyrolysis. No other catalyst material was required in these experiments. These structures contained iron and phosphorus, which are present in the derivative **1**. It was further shown that the resulting nanostructures are highly dependent on the starting material that was employed. Such unique iron-encapsulated carbon nanostructures may find a potential role in nanoscale applications. Further experiments are currently in progress to explore the pyrolysis behavior of other simple organometallic complexes.

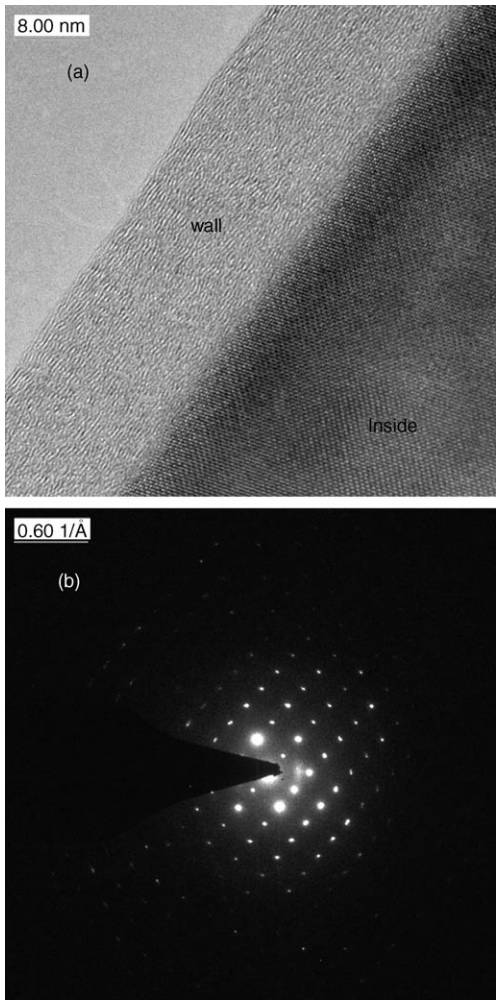

Figure 3. a) HRTEM image of a capsule wall and the material contained inside the capsule after annealing at 700 °C for 12 h; b) electron diffraction pattern originating from the material found inside the capsule shown in (a).

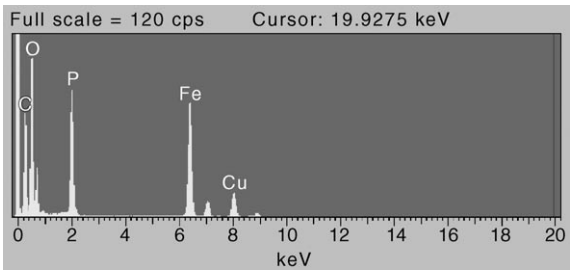

Figure 4. A typical EDS image of the filled nanocapsules indicating the presence of Fe and P within the interior of the capsules.

Experimental Section

All of the chemicals used in the experiments were bought from Merck and Fluka and were used as received without further purification. Complexes **1**[31] and **2**[32] were prepared according to the literature procedures. NMR data and CHN analysis provided proof of the purity of the complexes. Pyrolytic combustion experiments were performed in an alumina tube placed horizontally in a Carbolite furnace. The general morphology of the samples obtained was observed with a Philips CM200 FEG (operated at 120 kV) and a Philips CM 400 (operated at 200 kV) transmission electron microscope equipped with an energy-dispersive X-ray spectrometer. Samples for TEM were prepared by dispersing the material in 2-propanol and then placing them onto a copper grid coated with a holey carbon film.

For the pyrolysis experiments, complexes **1** and **2** were sealed under vacuum in a quartz tube. The tube was then placed in a furnace and heated at a rate of 10 °C min^{-1} up to 700 °C. The tube was maintained at 700 °C for 2 h and then allowed to cool back down to room temperature. The sealed tube was opened and no internal pressure was recorded. The soot was collected and stirred in concentrated HCl for 15 h and then further washed several times with deionized water. The sample obtained was then dried in an oven at 60 °C overnight. One sample was further annealed under an argon atmosphere at 700 °C for 12 h.

Keywords:

carbon · electron microscopy · iron · nanostructures · precursor synthesis

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Influence of the Substitution Pattern of Cp-Iron-Arene Salts in the Solid-State Synthesis of New Carbon Nanostructures

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A series of Cp-iron-arene hexafluorophosphate salts have been prepared and pyrolyzed under autogenous pressure. It was found that the resulting carbon nanostructures were highly dependent on the starting material. Even a small change in the substitution pattern of the arene ligand could result in different material. In addition to very short hollow carbon nanofibers, also called carbon nanocapsules, it was possible to prepare long homogeneous carbon fibers in quantitative yield, which incorporated iron phosphorus composite particles in remarkable continuous distances.

1. Introduction

In addition to single-walled and multiwalled carbon nanotubes,[1–4] various more or less related structures, including carbon nanohorns,[5–7] carbon nanospheres,[8–11] and onion-like carbon structures.[12,13] have been prepared. If these structures contain metals, they have additional potential as magnetic particles, contrast agents, protecting cloaks, and catalysts, and in other applications.[4,14–18] Despite their emerging applications such structures in addition to carbon nanotubes are often relatively difficult to produce in bulk compared to carbon nanotubes. Occasionally, they were produced only as byproducts during the preparation of carbon nanotubes.[10,19,20] Arc-discharge using metal-doped graphite rods,[6,21] pyrolysis of carbonizing mixtures,[22–24] or catalytically assisted chemical vapor deposition (CCVD) methods are some of the involved methods.[25–28] For example, the group of C. N. R. Rao reported first some CVD processes involving the pyrolysis of ferrocene in an open system with a flow of argon with or without a hydrocarbon source, which leads to carbon nanotubes.[29–31] Several of these procedures require relatively complex setups and can have limitations over the range of metals and the amount of filling. Another option to prepare these structures is the pyrolysis of different organometallic complexes in a sealed vessel under autogenous pressure, which can lead to carbon nanotubes,[32–35] carbon nanocables,[34,36] onions,[34,37] and microspheres.[35]

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Figure 1. Cp(Fe)arene salts.

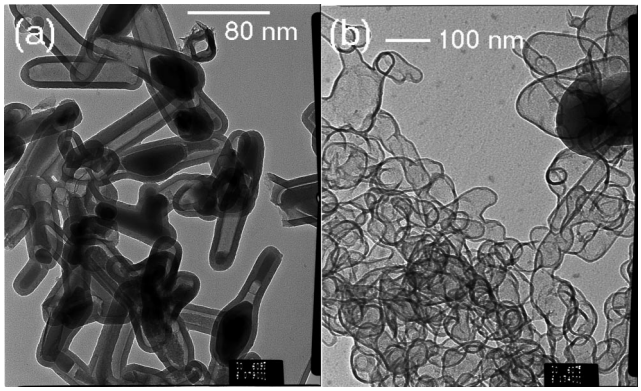
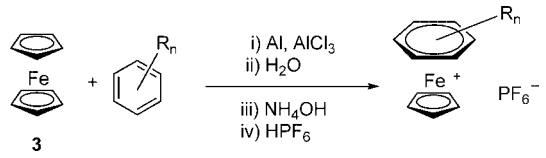


Figure 2. (a) TEM image of material from pyrolyzed complex **1** and (b) TEM image of material from pyrolyzed complex **2**.

Scheme 1. Preparation of Cp(Fe)arene Salts from Ferrocene[39,42]

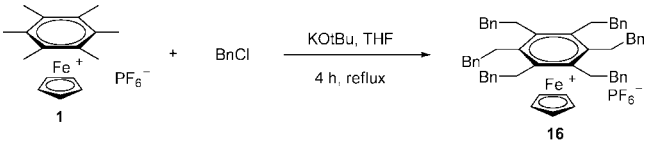


Recently, we found a straightforward method to prepare a novel nanocarbon structure, carbon nanocapsules filled with Fe−P composite, in near quantitative yield (Figure 2a).[38] The new particles were obtained via the simple pyrolysis of CpFe(arene) salt **1**[39] at 700 °C under autogenous pressure in a sealed vessel and can be described as short hollow carbon fibers.

In addition complex **2**[40] resulted in some form of coral carbon structure, whose picture is shown in Figure 2b.

Here an investigation on the influence of different substitution patterns of the starting complexes on the resulting material and functionalization studies of the obtained material will be presented.

Scheme 2. Preparation of Salt 16[43]



2. Results and Discussion

In addition to complexes **1**[39] and **2**[40] complexes **4**−**13**[39] and **14**[41] were prepared according to the literature as shown in Scheme 1. Starting with ferrocene, one Cp ligand can be simply exchanged with the desired arene in the presence of aluminum, aluminum chloride, and equimolar amounts of water at 100 °C after several hours. The desired salts were precipitated after workup by the addition of HPF_6. The salts chosen for this investigation are depicted in Figure 3.

In addition complex **16** was prepared according to Scheme 2 by the reported procedure of Astruc et al. by treating complex **1** with benzyl chloride in the presence of a strong base in THF under reflux.[43]

The complexes were then pyrolyzed under the same conditions reported for complex **1** for 2 h at 700 °C in an evacuated sealed quartz tube. Some of the resulting pyrolyzed material, which is similar to the observed nanocapsules from salt **1**, is depicted in Figure 4. However in the beginning ferrocene **3** was pyrolyzed at 700 °C, which resulted in the same observation recently reported by Coville et al.[35] Amorphous carbon in addition to some MWCNTs was obtained as the major product. This shows the considerable difference of this method compared to CVD processes, where ferrocene has been successfully used for the synthesis of MWCNTs.[28–31] The comparison of the two methods for the presented salts is not possible since these compounds cannot be sublimed. Only decomposition is observed, which makes them ideal for application in solid-state pyrolysis.

It is possible to see in Figure 4 that five analogues of salt **1** resulted in similar structures during the pyrolysis at 700 °C. The benzene analogue **4** also gave nanocapsules; however they were not completely developed and not separated from each other (Figure 4a). This material resembles some recently prepared nanocages by Holmes et al.[44] The cages were synthesized by the deposition of *p*-xylene over a Mo/Co catalyst in supercritical carbon dioxide. The toluene analogue **5** resulted in a few half-developed capsules (Figure 4b). The 1,2,3-trimethylbenzene salt **10** showed nearly the same result as salt

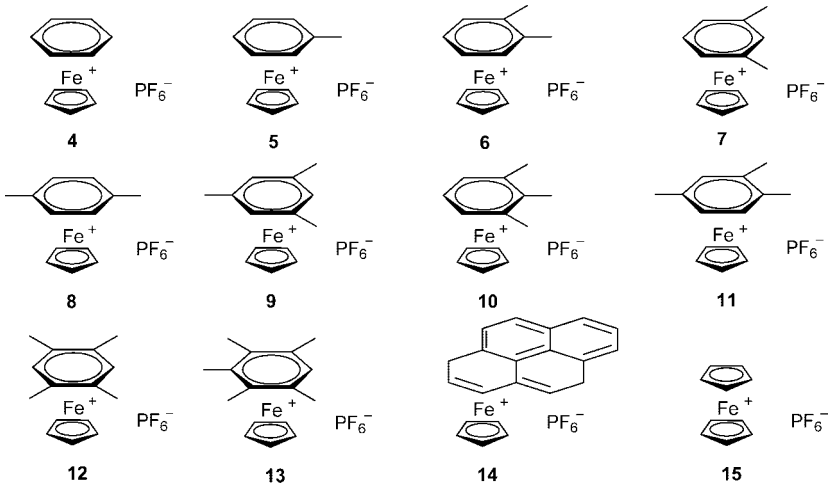


Figure 3. Salts prepared according to Scheme 1 (**1**−**14**) and purchased salt **15**.

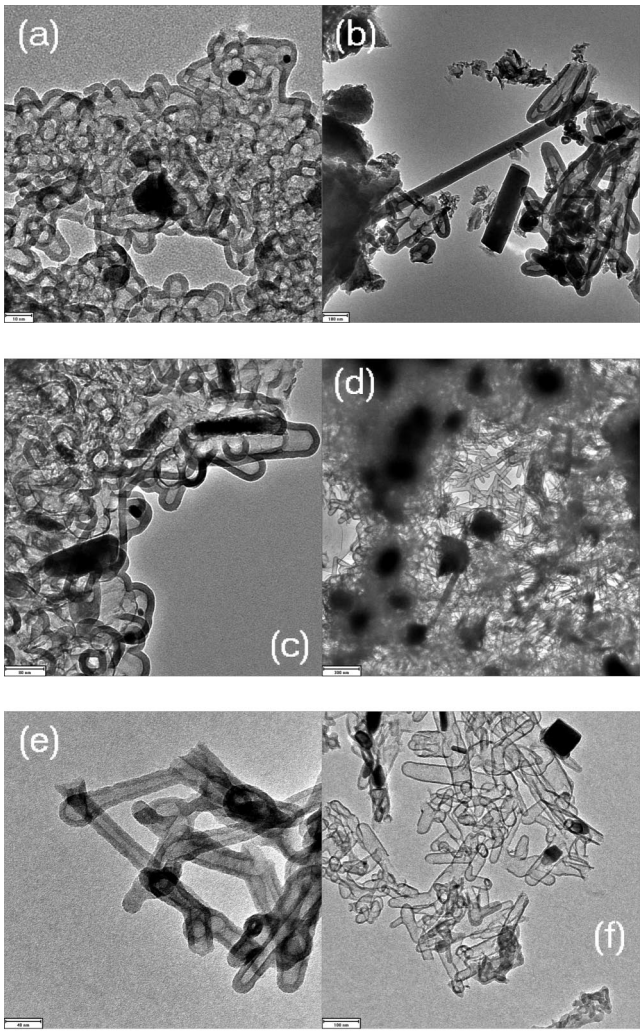


Figure 4. TEM images of pyrolyzed material at 700 °C for 2 h from (a) complex **4**, (b) complex **5**, (c) complex **10**, (d and e) complex **12**, and (f) complex **13**.

5 (Figure 4c), while the 1,2,4,5-tetramethylbenzene complex **12** gave nanocapsules in good yield as obtained by hexamethylbenzene complex **1** (Figure 4d,e). However, a small amount of amorphous carbon was present and the quality of the capsules was slightly lower compared to those from salt **1**. Finally the pentamethylbenzene salt **13** resulted in capsules that had a far smaller wall thickness compared to complex **1** (Figure 4f).

Although very similar to the complexes presented so far, the 1,2-dimethylbenzene salt **6** and its 1,3- and 1,4-analogues **7** and **8** gave only amorphous carbon as the major product when pyrolyzed at 700 °C. Similar results were found by the pyrolysis of the 1,2,4-trimethylbenzene salt **11**. Additionally, the arene complexes were also pyrolyzed at 500 °C for 2 h. All arene salts gave mainly amorphous carbon, except complexes **1** and **13**, which resulted in nanocapsules, however with low quality.

A remarkable exception is the 1,3,5-trimethylbenzene complex **9**. Pyrolysis of this complex at 500 °C resulted in less developed nanocapsules, as shown in Figure 5a. However, when the salt was pyrolyzed at 700 °C, carbon fibers in nearly quantitative yield were obtained (Figure 5b,c,d). These fibers (for HRTEM see the Supporting Information) had a diameter between 35 and 280 nm with a length varying between 3.2 and 10 μm. Nearly all of the fibers, like the nanocapsules in our previous study,[38] had Fe−P nanoparticles incorporated, which were analyzed by EDX (see the Supporting Information).

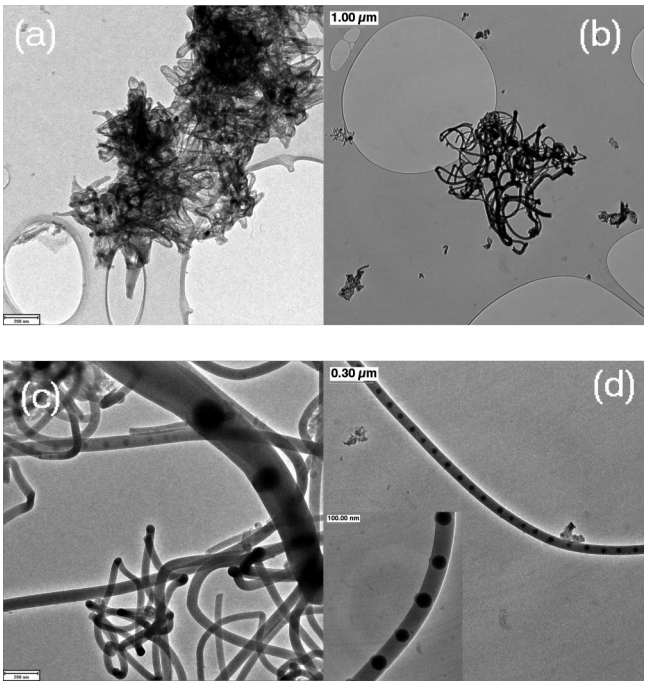


Figure 5. TEM images of pyrolyzed material of complex **9** (a) at 500 °C and (b, c, and d) at 700 °C.

Remarkable is the regular spacing of the particles. The distance between two particles inside a fiber is nearly always double the diameter of the fiber. In most of cases the diameter of a particle was found to be 80% of the diameter of the fibers; however sometimes a few particles were found having a diameter larger than the fiber they were incorporated in. One should point out at this stage the dramatic effect that the difference of the starting material has comparing for example the results obtained from the 1,3,5-trimethylbenzene salt **9** and the 1,2,3-trimethylbenzene salt **10**.

Some of the above-described complexes, which gave mainly amorphous carbon in the pyrolysis experiments, showed some other well-defined nanostructures, although in a low yield between 5% and 10% estimated from TEM analysis, and are presented in Figure 6.

Complex **15** resulted at 700 °C in a small amount of carbon microspheres (Figure 6a) with a diameter up to 800 nm. Complex **16** resulted at 500 °C in microspheres with a diameter of up to 1200 nm (Figure 6b). With complex **5** at 500 °C some well-defined microhorns were found with a length between 4300 and 5300 nm and a diameter of 540 nm. The walls were 75 nm thick (Figure 6c). The pyrolysis of salt **11** at 500 °C also led to microhorns with an average length of 3700 nm and a diameter of 520 nm. The walls were 32 nm thick (Figure 6d−f). On the surface some Fe−P nanoparticles can be observed, which was confirmed by EDX (see the Supporting Information). In addition when complex **16** was pyrolyzed, some nanodonuts were detected (Figure 6f). This form has been recently found in material from asteroids.[45]

In order to evaluate if phosphor is necessary for obtaining nanostructured material, complex **1** with a BF_4 counteranion[39] was prepared and pyrolyzed at 700 °C for 2 h. Although no well-defined nanocapsules were observed, some coral-like nanostructure was found (see Figure 7). This indicates that the anion has an influence on the resulting material.

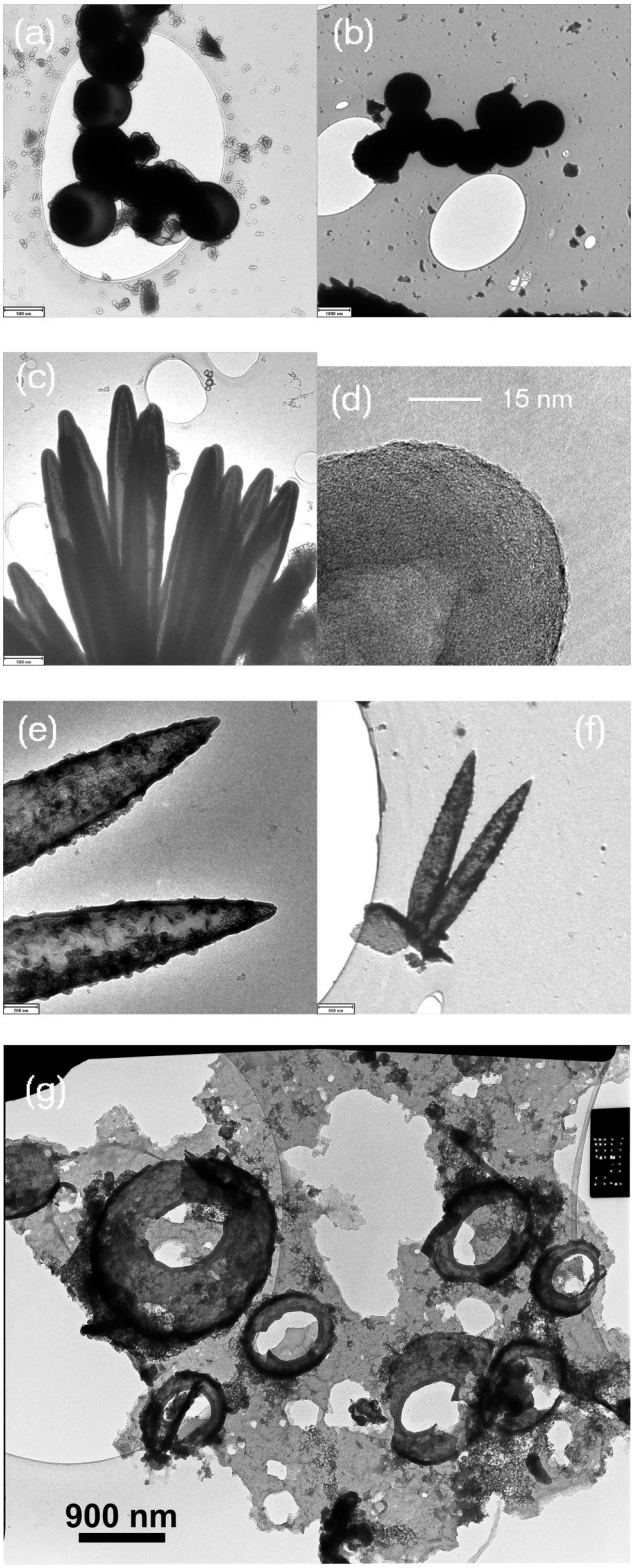


Figure 6. TEM images of pyrolyzed material of (a) complex **15** at 700 °C, (b) complex **16** at 500 °C, (b, c) complex **5** at 500 °C, (d, e, and f) complex **11** at 500 °C, and (g) complex **16** at 900 °C.

3. Conclusions

It was possible to show that novel carbon nanostructures are accessible via the pyrolysis of Cp-Fe-arene hexafluorophosphate salts. In the case of complexes **1** and **9** the material was obtained in nearly quantitative yield. In addition several new well-defined carbon nanostructures were found. It was also shown that even the smallest change in the substitution pattern in the starting arene salt had a dramatic effect on the result. Nanocapsule-related material was obtained from complexes **4**, **5**, **10**, **12**, and **13** at 700 °C after 2 h and complex **9** at 500 °C. Long nanofibers were obtained from complex **9** at 700 °C after 2 h, and short tubular structures were prepared from complex **5**. Spherical structures were found with complex **15** at 700 °C and complex **16** at 500 and 900 °C. In all samples no fluoride was observed, which can be explained by the use of sealed quartz tubes. Clearly the fluoride must have reacted with this material. However, to predict a resulting nanostructure from a certain starting material and to understand the mechanism of the pyrolysis remain difficult, and as shown, no obvious trend can be observed. The presented nanostructured material could have, for example, high potential for gas-storage media,[46,47] Li-intercalation materials for batteries,[48] and cold electron field emitters.[49]

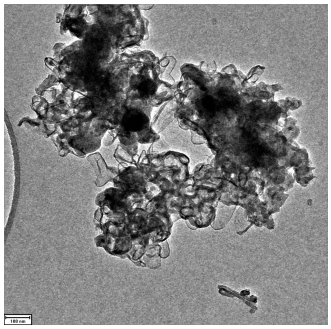


Figure 7. TEM images of pyrolyzed material of complex **1** with a BF_4 counteranion.

4. Experimental Section

Salts **1**,[39] **2**,[40] **3**−**13**,[39] and **14**[41] were prepared according to a literature procedure.[42] Salt **1** with BF_4 as a counteranion was prepared according to the literature.[39] Salt **15** was purchased from Aldrich. Salt **16** was prepared according to the literature.[43] Pyrolytic combustion experiments were performed in an alumina work tube placed horizontally in a Carbolite furnace. General morphology of the samples obtained was observed with a Philips CM200 FEG (operated at 120 kV) and a Philips CM 400 (operated at 200 kV) transmission electron microscope equipped with an energy-dispersive X-ray spectrometer (EDS). Samples for TEM were prepared by dispersing the material in 2-propanol and then placing it onto a copper grid coated with a holey carbon film.

For the pyrolysis, complexes were sealed under vacuum in a quartz tube. The latter was placed in a furnace and heated at a rate

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of 10 °C/min to 500, 700, or 900 °C. It was then kept at that temperature for 2 h and left to cool to rt. The sealed tube was opened, and no internal pressure was found. The soot was collected and stirred in concentrated HCl for 15 h and was further washed several times with deionized water. The sample so obtained was dried in an oven at 60 °C overnight.

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Supporting Information Available: This material with EDX scans and additional TEM images is available free of charge via the Internet at http://pubs.acs.org.

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